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LABORATORY TESTS IN GENERAL PRACTICE

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Because the number of available laboratory tests is bewildering, my discussion will deal only with a few of the simpler procedures which are useful and which can be carried out effectively in a small hospital, in a small group or even in an individual physician's office. The tests, including the series of tests of function, have been chosen for the purpose of recommending only those which have been introduced in the last few years and have proved helpful. A number are primarily diagnostic, while others are employed to evaluate the results of therapy or to study the progress of the disease. In other words, they are tests of diagnosis and tests of progress.

For this discussion certain tests of hepatic function, examinations of the blood and the urine and the value of the erythrocyte sedimentation rate will be considered.

TESTS OF HEPATIC FUNCTION

Tests of hepatic function are of considerable practical use if the wide variety of known hepatic functions is borne in mind and if it is remembered that of these functions some are more likely to be disturbed in a given type of disease than are others. Therefore, no one test can possibly be expected to reveal all the dysfunctions.[1] Even under well controlled conditions there is often a disassociation of results when a number of similar tests are made. Obviously it would be impossible to employ all the tests of hepatic function which I shall mention in the study of a given patient; consequently the test to be employed must be carefully selected to suit the need.[2]

One of the early and still useful tests of hepatic function utilizes the dye-excreting capacity of the liver in which the degree of retention of dye in the blood indicates the degree of hepatic dysfunction. A number of different dyes have been proposed, but bromsulfalein has found the widest acceptance. Originally the test [3] consisted of the intravenous administration of 2 mg. of bromsulfalein per kilogram of body weight. A recent modification of this test consists of the intravenous administration of 5 mg. of bromsulfalein per kilogram of body weight, and only 1 blood sample for comparison is withdrawn in forty-five minutes.[4] These two tests are both sensitive and reliable for the detection of impairment of hepatic function and give but few false positive reactions. Usually they are positive when relatively minor hepatic damage is present. They are easy of performance and require only one, two or at most three venipunctures. The disadvantages of these tests are that they are useless when the patient is jaundiced, and when the larger 5 mg. per kilogram dose of bromsulfalein is given there may be occasional reactions, consisting principally of transient headache, the feeling of faintness, and in some cases a chill which occurs from forty-five to sixty minutes after the injection of the dye.[4c] The headache may persist for several hours, but there has been no prolonged or unfavorable after-effect. The method in which the 2 mg. dose is employed is less sensitive as a measure of the degree of hepatic dysfunction than the method in which the 5 mg. dose is used. These two tests are particularly useful in the preoperative study of patients with cholelithiasis, thyroid disease, and when possible hepatocellular abnormality is not accompanied by jaundice.

Another recently described test of hepatic function is the cephalin-cholesterol flocculation test.[5] The liver plays an important role in protein metabolism and in man, at least, is concerned with the deaminization of amino acids, the formation of urea and the formation of fibrinogen and perhaps other blood proteins. With dysfunction of the liver, alterations of these as well as of other proteins occur. Other tests based on the alterations of protein metabolism include the Takata-Ara reaction and Gray's colloidal gold test. Because of technical difficulties they are not so widely used as the cephalin-cholesterol flocculation test. In the latter test when the emulsion of cephalin-cholesterol is added to the serum of patients with hepatocellular damage a flocculation occurs. In the performance of this test there are several precautions which must be observed.[6]

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Because of lack of space this article has been abbreviated in THE JOURNAL. The complete paper will be found in the author's reprints which the author will be pleased to send on request.

1. Yardumian, K. Y., and Weisband, B. J.: The Cephalin Cholesterol Flocculation Test in Liver Disease, Am. J. Clin. Path. **13:** 383-392 (Aug.) 1943.

2. Israel, H. L., and Reinhold, J. G.: Detection of Cirrhosis and Other Diseases of the Liver by Laboratory Tests, J. Lab. & Clin. Med. **23:** 588-596 (March) 1938.

3. Rosenthal, S. M., and White, E. C.: Clinical Application of the Bromsulphalein Test for Hepatic Function, J. A. M. A. **84:** 1112-1114 (April 11) 1925.

4. (*a*) Mateer, J. G.: Personal communication to the author. (*b*) Mateer, J. G.; Baltz, J. L.; Marion, D. F.; Hollands, R. A., and Yagle, E. M.: A Comparative Evaluation of the Newer Liver Function Tests, Am. J. Digest. Dis. **9:** 13-29 (Jan.) 1942. (*c*) Mateer, J. E.; Baltz, J. L.; Marion, D. F., and MacMillan, J. M.: Liver Function Tests, J. A. M. A. **121:** 723-728 (March 6) 1943.

5. (*a*) Hanger, F. M.: The Flocculation of Cephalin-Cholesterol Emulsions by Pathological Sera, Tr. A. Am. Physicians **53:** 148-151, 1938; (*b*) Serological Differentiation of Obstructive from Hepatogenous Jaundice by Flocculation of Cephalin-Cholesterol Emulsions, J. Clin. Investigation **18:** 261-269 (May) 1939.

6. Neefe, J. R., and Reinhold, J. G.: Photosensitivity as a Cause of Falsely Positive Cephalin-Cholesterol Flocculation Tests, Science **100:** 83-85 (July 28) 1944.

Exposure to bright sunlight increases the sensitivity of the reaction and produces false positive reactions in a large number of cases. For this reason the test should be carried out away from strong light. The antigen emulsion can be stored for a short time only, and it must be stored in the dark.[7]

The cephalin-cholesterol flocculation test also has the advantage that it is sensitive and reliable and that it can be used equally well in the study of jaundiced and of nonjaundiced patients. It is roughly quantitative and requires only one venipuncture. Its disadvantages are that the technic and the reagents must be exact, that occasional false positive reactions are encountered in allergic states, during pregnancy and in the neonatal period,[8] and that the final interpretation of the test takes forty-eight hours. The cost of the test is high because new cephalin-cholesterol emulsions must be prepared for each day's testing.

Another important function of the liver is that of detoxification of poisons, in which by processes of oxidation and conjugation toxic substances are changed to relatively less toxic compounds which are subsequently eliminated in the bile and urine. It is on this basis that the hippuric acid test was devised [9] and has been used for many years with such excellent success.[10] Sodium benzoate given to a patient is conjugated with aminoacetic acid and is excreted as hippuric acid in the urine. The rate of synthesis of hippuric acid is governed by the ability of the liver to produce aminoacetic acid. In certain types of hepatic dysfunction the urinary output of hippuric acid will diminish owing to the lack of aminoacetic acid production. The excretion of the end product of detoxification is dependent on intact renal function; hence before reliance can be placed on the results of this test one must have assurance that the renal function is satisfactory. There are two methods for the performance of the hippuric acid test, the oral method [9] and the intravenous method.[11] This test has the following advantages: It is reliable; it can be used when the patients are jaundiced or nonjaundiced;[13] it tests the detoxifying function of the liver, and it is extremely sensitive and detects even minor hepatic damage. This method is inexpensive. The disadvantages of both the intravenous and the oral method are essentially the same. In gastric retention or delay of emptying there is diminished absorption of the orally ingested sodium benzoate, and in the presence of renal damage, incomplete emptying of the bladder or dehydration, the urinary flow is not sufficient to obtain accurate estimates. With the oral hippuric acid test there is also occasional nausea and vomiting. The oral method is less sensitive than the intravenous method and consumes approximately four hours of the patient's time as against one hour with the intravenous method.

Bilirubin is the chief pigment of human bile and is derived from hemoglobin by a process of hydrolysis. The adequacy with which this hemoglobin product is metabolized and excreted by the hepatic cells can be estimated from the determination of the serum bilirubin in the blood. The determination of the icterus index is a much simpler procedure and has essentially the same advantages and disadvantages as the more technically difficult determination of the serum bilirubin. The test has as its advantages that it does indicate the degree of jaundice, and when used serially, accurately determines an increase or decrease of jaundice. Its disadvantages are that it is not a direct test of hepatic function and that its usefulness is limited principally to jaundiced patients.

From a practical standpoint there are several things which should be reviewed. In jaundiced patients tests of hepatic function are used to determine whether the jaundice is obstructive or hepatocellular in origin, and in nonjaundiced patients to determine the extent of hepatocellular damage in relation to the coincident disease.

While tests of hepatic function are not absolutely reliable guides for the differentiation of obstructive from hepatocellular jaundice,[14] there is evidence that patients with early jaundice who show strongly positive reactions to the tests of hepatic function have jaundice that is hepatocellular, while those who show slight or negative reactions have obstructive jaundice.[15] In this connection one can use sensitive tests of hepatic function reactions to which are positive with minor degrees of hepatic damage and less sensitive tests reactions to which are positive only in advanced states of hepatic dysfunction.

In jaundiced patients a continued rise in serum bilirubin or icterus index levels would indicate continued obstruction or perhaps increasing hepatocellular damage. The best information as to the state of the functional activity of the liver in cases of jaundice can be gained from a consideration of the value for the serum bilirubin and of its daily variation and a knowledge of the anatomic changes which these may represent.[16]

In nonjaundiced patients with cirrhosis positive results are usually obtained with both the sensitive and the less sensitive tests.

Tests of hepatic function are of lesser importance in diagnosis than they are in treatment. This is particularly true when one considers the role of the liver in infections in relation to surgical diseases such as thyrotoxicosis and certain lesions of the gastrointestinal and biliary tract, as well as their use in the control of treatment with hepatotoxic drugs. Positive reactions may occur during the course of infection,[8] and in infectious disease of children have been assumed to indicate evidence of hepatic damage,[17] particularly in severe disease or in disease with complications. In the interpretation of the more sensitive tests of hepatic

7. Neefe and Reinhold.[6] Mateer.[7a]
8. Wade, L. J., and Richman, E. E.: The Cephalin-Cholesterol Flocculation Test, J. Lab. & Clin. Med. **30:** 6-13 (Jan.) 1945.
9. Quick, A. J.: The Synthesis of Hippuric Acid: A New Test of Liver Function, Am. J. M. Sc. **185:** 630-635 (May) 1933; Clinical Value of the Test for Hippuric Acid in Cases of Disease of the Liver, Arch. Int. Med. **37:** 544-556 (March) 1936.
10. Boyce, F. F., and McFetridge, E. M.: Studies of Hepatic Function by the Quick Hippuric Acid Test, Arch. Surg. **37:** 401-455 (Sept.) 1938.
11. Quick, A. J.: Intravenous Modification of the Hippuric Acid Test for Liver Function, Am. J. Digest. Dis. **6:** 716-717 (Dec.) 1939.
13. Snell, A. M., and Plunkett, J. E.: The Hippuric Acid Test for Hepatic Function: Its Relation to Other Tests in General Use, Am. J. Digest. Dis. & Nutrition **2:** 716-721 (Feb.) 1936.
14. Pohle, F. J., and Stewart, J. K.: The Cephalin-Cholesterol Flocculation Test as an Aid in the Diagnosis of Hepatic Disorders, J. Clin. Investigation **20:** 241-247 (March) 1941.
15. Kirschner, P. A., and Glickman, S. I.: The Cephalin Flocculation Test in Jaundice, J. Lab. & Clin. Med. **28:** 1721-1724 (Nov.) 1943. Rosenberg, D. H., and Soskin, S.: Azorubin S. Test of Liver Function: Evaluation with Comparative Study of Bromsulphalein and Hippuric Acid Tests, Ann. Int. Med. **13:** 1644-1654 (March) 1940. Wade and Richman.[8]
16. Snell, A. M., and Magath, T. B.: The Use and Interpretation of Tests for Hepatic Function: A Clinical Review, J. A. M. A. **110:** 167-174 (Jan. 15) 1938.
17. Meneghello, J., and Drinberg, M.: Intravenous Hippuric Acid Test in Infectious Diseases of Children, Am. J. Dis. Child **66:** 103-113 (Aug.) 1943.

V 13
1946

function one must recall that elderly persons will manifest some evidence of hepatic dysfunction by any or, perhaps, by all of the tests listed.[18]

In preoperative management one must consider the possibility of hepatic dysfunction not only in the initial state of the patient but also in regard to the anticipated trauma of operation, the anoxia incident to anesthesia and blood loss. The toxic effects of certain anesthetic agents must also be considered. For these reasons it is imperative that the preoperative estimation as well as the postoperative study of hepatic function should be made for all seriously ill patients.[19]

In the course of treatment with hepatotoxic drugs it is advisable to make tests of hepatic function periodically. This is particularly indicated when patients are undergoing prolonged or intensive therapy with sulfonamide drugs. Intensive therapy or prolonged use of the drug does not appear necessary to produce some evidence of hepatic damage.[20]

In summary, evidence of increased hepatic damage indicates an unfavorable prognosis, while evidence of improved hepatic function denotes diminution in the severity of the disease process.[21] Because of the dissociation of functions it is wise to employ more than one test, preferably a sensitive and a less sensitive test. While it is impossible to make a diagnosis through the use of tests of hepatic function alone, the physician who properly considers the results of these tests together with the history and physical examination will be rewarded by an increase in the accuracy of his diagnoses and prognoses.

BLOOD STUDIES

There is a large number of office procedures available for the examination of the blood. From them I should like to select only those which I feel are most essential in office practice.

The coagulation time is of particular importance in connection with the pathogenesis and differential diagnosis of the primary and secondary hemorrhagic diseases. Of the various methods for determining coagulation, that of Lee and White is as simple as any.

The bleeding time is the time required for a small cut to cease bleeding. Duke's method is satisfactory.[22a] These tests are of particular value for those patients for whom an operation is contemplated, because then one can estimate the ability of the patient's blood to clot and retract in a normal manner.

The technic and methods for erythrocyte and leukocyte counts are generally known. There are a few precautions and considerations, however, which might be discussed briefly. In the first place, the instruments to be used must be scrupulously cared for and satisfactorily clean. Further, one must recall that the normal error of an erythrocyte count may be as much as plus or minus 16 per cent.[23] In evaluating the erythrocyte and leukocyte count one must also take into consideration the concentration of the blood and the state of its dilution.

I should like to emphasize the extreme importance of blood smear examinations, in which the nature and character of the leukocytes are noted. Of all blood examinations, the intelligent study of the stained film will yield the most diagnostic information.

The polymorphonuclear leukocyte probably deserves most attention from the standpoint of prognosis. The percentage of neutrophils represents the severity of the infection, while the total white blood cell count indicates the patient's power of resistance.[24] These two facts have been expressed in a number of ways over the past forty years. Many numerical relationships between the total count, the leukocyte count, the lymphocyte and the monocyte percentages have been suggested. Arneth [25] has grouped the neutrophils into five classes according to the number of lobes which their nuclei possess. Farley, St. Clair and Reisinger [26] modified the Arneth count to the point where they use only two classifications of neutrophils—the filamented and the nonfilamented cells. The nonfilamented cells are immature forms, and of these the upper limit is approximately 16 per cent, although the average normal proportion is not greater than 6 to 9 per cent of the total white cell count. The presence of many nonfilamented forms denotes acute infection or other irritation in the body which has stimulated the activity of the bone marrow.

Another change found in the polymorphonuclear cells in extremely toxic states is the moth-eaten irregular cell outline, a replacement of the neutrophilic granules by large dark irregular basophilic granules which often are so numerous as to fill the entire cell.[26a] An increasingly toxic smear or one with an increase in nonfilamented forms usually indicates an unfavorable outcome, while the smear in which these manifestations gradually diminish usually presages a satisfactory recovery.

Occasionally bone marrow biopsies must be resorted to in order to establish the nature of some blood dyscrasias. The interpretation of these preparations should be left to one with considerable experience in this field.

STUDIES OF URINE

The urine can profitably be investigated as an office procedure, but there are several precautions which should be considered in its examination. While it is perfectly satisfactory to do qualitative tests on single urine specimens, quantitative tests should be run on a portion of a twenty-four hour sample if they are to be of greatest value. During the period of collection the urine should be passed into a clean vessel and kept

18. Rafsky, H. A., and Newman, B.: Liver Function Tests in the Aged, Am. J. Digest. Dis. **10:** 66-69 (Feb.) 1943.

19. Boyce and McFetridge.[10] Casten, D.; Bodenheimer, M., and Barcham, I.: A Study of Plasma Protein Variations (and Hepatic Function) in Surgical Patients, Ann. Surg. **117:** 52-73 (Jan.) 1943.

20. Andersch, M. A.: Hepatic Damage Associated with Sulfonamide Therapy in Infants and Children: II. Changes in Liver Function Test During Sulfonamide Therapy, Ann. Int. Med. **19:** 622-628 (Oct.) 1943.

21. Hoffbauer, F. W.; Evans, G. T., and Watson, C. J.: Cirrhosis of the Liver with Particular Reference to Correlation of Composite Liver Function Studies with Liver Biopsy, M. Clin. North America **29:** 363-388 (March) 1945.

22a. Duke, W. W.: The Relation of Blood Platelets to Hemorrhagic Disease: Description of a Method for Determining the Bleeding Time and Coagulation Time and Report of Three Cases of Hemorrhagic Disease Relieved by Transfusion, J. A. M. A. **55:** 1185-1192 (Oct.) 1910.

23. Magath, T. B.; Berkson, J., and Hurn, M.: The Error of Determination of the Erythrocyte Count, Am. J. Clin. Path. **6:** 568-579 (Nov.) 1936.

24. Sondern, F. E.: The Value of the Differential Leucocyte Count in Diagnosis, Am. J. M. Sc. **132:** 889-891 (Dec.) 1906.

25. Arneth, J.: Die neutrophilen weissen Blutkörperchen bei Infektions-Krankheiten, Jena, Gustav Fischer, 1904, p. 37, plate 8.

26. Farley, D. L.; St. Clair, H., and Reisinger, J. A.: The Normal Filament and Non-Filament Polymorphonuclear Neutrophil Count, Its Practical Value as a Diagnostic Aid, Am. J. M. Sc. **180:** 336-344 (Sept.) 1930.

26a. Rosenthal, N., and Sutro, C. J.: The Blood Picture in Pneumonia with Special Reference to Pathologic Changes in the Neutrophils, Am. J. Clin. Path. **3:** 181-197 (May) 1933.

in a cool place. The large twenty-four hour specimen is mixed thoroughly and a sample removed for examination. Random urine specimens obtained several hours after a meal are the most likely to contain abnormal substances, while the usually accepted first specimen of the morning is least likely to contain them.

TABLE 3.—*Office Urinalysis*

Qualitative Tests	Function Tests	Microscopic
Albumin	Intravenous phenolsulphonphthalein	Organized sediments:
Sugar	Mosenthal concentration	Casts
Acetone	Pituitrin concentration	Leukocytes
Urobilinogin		Erythrocytes
Bilirubin		

The urine should be examined while fresh, as decomposition sets in rapidly, especially if the specimen is kept in a warm place. The office examinations which I should consider most important are listed in the accompanying table.

The albumin test should always be done on urine which is clear or has been clarified by filtration or centrifugation. For practical purposes the ring or contact test is satisfactory. Glycosuria may be detected in any one of a number of ways. For office procedure the Clinitest tablets can be recommended as satisfactory.[27] The results of this test are chiefly qualitative, but a rough quantitative estimation can be made as well.

Under normal conditions bilirubin enters the intestine in the bile and is broken down to urobilinogen, which through a process of oxidation is transformed into urobilin. Thus urobilin and urobilinogen are present in the stools of normal persons and in traces in bile and in urine. A portion of the urobilinogen formed in the intestine is reabsorbed into the portal blood stream and carried to the liver, where it is reconverted into bilirubin or some other pigment complex. This cycle is termed the enterohepatic circulation of bile pigment. In patients with excessive blood destruction or hepatocellular damage this circulation is interrupted, and urobilinogen is excreted in the urine. Urobilinogen determinations can be carried out either on a qualitative or on a quantitative basis.[28] Steigmann, Popper and Meyer[29] have studied the urine bilirubin

TABLE 4.—*Urine, Bilirubin and Urobilinogen*[29]

	Urine Bilirubin	Urine Urobilinogen
Hemolytic jaundice.....	Negative	Increased
Complete obstructive jaundice	Positive	Negative
Partial obstructive jaundice...	Positive	Variable; may be increased after release of obstruction
Parenchymatous jaundice.....	Positive	Much increased early; little increased late

and urobilinogen in a large number of cases of hepatic disease with the following results:

About two thirds of the cases studied were diagnosed accurately by means of this single examination, and prolonged observation of these two tests increased the percentage of correct diagnosis to 79 per cent.[29]

27. Kasper, J. A., and Jeffrey, I. A.: A Simplified Benedict Test for Glycosuria, Am. J. Clin. Path. (technical section) **14:** 117-121 (Nov.) 1944.

28. Watson, C. J.: Studies of Urobilinogen: I. An Improved Method for the Quantitative Estimation of Urobilinogen in Urine and Feces, Am. J. Clin. Path. **6:** 458-475 (Sept.) 1936.

29. Steigmann, F.; Popper, H., and Meyer, K. A.: Liver Function Tests in Clinical Medicine (Especially Jaundice), J. A. M. A. **122:** 279-285 (May 29) 1943.

There are innumerable tests of renal function which have been advocated from time to time. Of this number the intravenous phenolsulphonthalein test, the Mosenthal concentration test and the recently described pituitrin concentration test[30] are of value as office procedures. Other tests in which blood chemical studies are necessary are of inestimable value in the study of kidney diseases but must be considered as procedures adapted particularly to a hospital practice rather than for office use.

A concentration method which is apparently equal to the Mosenthal test in reliability is that by which renal concentration is measured after the injection of posterior pituitary substance. The test is performed as follows: The patient is required to empty the bladder, and this specimen is saved. Then he is given 1 cc. of obstetrical or 0.5 cc. of surgical pituitrin, after which the urine is collected every hour for two hours. The specific

TABLE 5.—*Comparison of Pitressin and Mosenthal Concentration (Ten Units of Pitressin)**

	Systolic Blood Pressure			Urinary Specific Gravity					
		After Pitressin			After Pitressin		Mosenthal		
Case	Initial	1 Hr.	2 Hr.	Initial	1 Hr.	2 Hr.	Low Day	High Day	Night
1	198	218	212	1.011	1.006	1.008	.....	.....	.....
2	198	188	178	1.003	1.009	1.015	1.005	1.010	1.010
3	146	156	158	1.004	1.010	1.018	1.003	1.015	1.010
4	128	118	110	.....	1.022	1.022	1.022	1.024	1.027
5	134	138	126	1.008	1.015	1.017	1.011	1.020	1.008
6	110	118	126	1.002	1.016	1.018	1.005	1.013	1.009
7	158	128	140	1.016	1.020	1.017	1.017	1.026	1.018
8	158	150	168	1.003	1.009	1.014	1.011	1.017	1.014
9	168	170	154	1.013	.....	1.015	1.013	1.017	1.015
10	122	114	118	1.012	1.020	1.027	1.015	1.025	1.015
11	162	142	142	1.003	1.013	1.018	1.010	1.023	1.025
12	176	154	154	1.018	1.015	1.018	1.016	1.021	1.007
13	194	174	178	1.010	1.012	1.011	1.013	1.020	1.009
14	172	142	152	1.014	1.010	1.015	1.008	1.016	1.008
15	166	166	122	1.025	1.021	1.024	1.017	1.025	1.021
16	142	124	126	1.018	1.016	1.021	1.006	1.019	1.013
17	184	166	174	1.021	1.020	1.025	1.027	1.027	1.027
18	122	102	114	1.021	1.021	1.021	1.010	1.024	1.023
19	210	182	204	1.003	1.016	1.015	.....	.....	.....
20	182	204	176	1.011	1.017	1.022	.....	.....	.....
21	154	150	152	1.017	1.016	1.010	1.018	1.024	1.017
22	118	114	122	.....	1.010	1.011	1.011	1.017	1.011
23	196	212	212	1.017	1.005	1.010	1.003	1.013	1.015
24	162	142	150	1.007	1.012	1.016	1.007	1.017	1.009
25	176	184	188	1.015	1.010	1.015	1.005	1.017	1.015

* Bailey, L. J.: Unpublished data.

gravity is determined for each specimen so collected. Nothing is to be given by mouth until the test is completed. The concentrating action is probably due to the antidiuretic action by reabsorption of fluid from the tubules. Normally patients during this test will excrete urine with a specific gravity of 1.023 or more. The contraindications for this test include severe oliguria, pregnancy, angina or myocardial infarction, epilepsy, hypersensitivity to the drug and arteriosclerotic heart disease with angina.[30] It is particularly indicated in patients with congestive heart failure and edema, and it may be used with unprepared patients as well as with uncooperative patients. It may likewise be used for patients with edema and in surgical cases in which it is undesirable for one reason or another to restrict fluids.

THE VALUE OF SEDIMENTATION RATE

The sedimentation test is a laboratory procedure of considerable historical interest and dates back to the period of bleeding or leeching of patients for various

30. Sodeman, W. A., and Engelhardt, H. T.: A Renal Concentration Test Employing Posterior Pituitary Injection, J. A. M. A. **122:** 1070-1072 (Aug. 14) 1943.

V 13
1946

diseases. It was noted that a particularly rapid settling of the lower red cell layer would occur frequently. This phenomenon was later utilized by Fahraeus[31] in 1918 as a test of pregnancy. However, it soon was discovered that this test was not specific as a test for pregnancy, because a number of disease states not related to pregnancy were associated with rapid settling of the erythrocytes. As a consequence, this test was discontinued for the diagnosis of pregnancy. In subsequent investigations, it was found that it could be of considerable value in the diagnosis and prognosis of disease. It is a simple test, requiring addition of an anticoagulant to venous or capillary blood; this blood is then placed in a vertical glass tube. The rate of fall of the erythrocyte layer is measured.

The great majority of sedimentation tests in use today are modifications of this procedure. In the first of these the fall of blood in a given period of time may be measured, is utilized,[32] or—by the opposite principle—the time which the blood takes to fall a given distance is determined.[32a] Whichever of these two procedures or their modifications is used, the results appear to be reasonably concordant. There are various factors which render the test unreliable,[33] but discussion of them cannot be undertaken at this time. Certain physiologic factors should be kept in mind in the interpretation of this test. For instance, the sedimentation rate is more rapid in women than in men; there is an increase of the rate in pregnancy after the first few months, with the peak recurring at parturition. The rate then gradually returns to normal during the puerperium. Among children excitement causes some increase.[33a] There are several technical factors which should be considered for the proper performance of the test. For instance, venous stasis during the withdrawal of the blood should be avoided, the test should be run within two hours after withdrawal of the blood, and as an anticoagulant ammonium and potassium oxalate should be used.[33b] The column of blood should be placed in an absolutely perpendicular position, and before the tube is filled agitation of the blood must be thorough and complete. Normal values for this test will vary somewhat with the different methods.

In addition to pregnancy there are two definite types of disease in which the sedimentation rate is elevated, inflammation and malignant growths. This test is of considerable value in the differential diagnosis of many inflammatory lesions. In acute appendicitis the sedimentation rate is normal in its early stage, while in acute salpingitis it is distinctly elevated.[34] Other benign pelvic lesions such as chronic salpingitis and abscess of Bartholin's gland, will also produce elevated rates, as will tuberculosis, either pulmonary or extrapulmonary. Most benign pelvic tumors, such as leiomyomas of the uterus, have essentially normal values.[34] In clinically benign pelvic tumors an elevated sedimentation rate should stimulate further search for complicating disease such as superimposed infection or malignant growths.[35] In coronary artery occlusion with infarction of the myocardium there is a rise in the sedimentation rate which begins shortly after infarction and subsides to normal within six to twelve weeks after the initial attack.[34] This test is also of some value in the differentiation of benign from malignant gastrointestinal disease. Benign intestinal lesions usually have a normal sedimentation rate, while those that are malignant will be accompanied by an elevation.[36] In certain chronic diseases, as infectious arthritis, and in acute rheumatic fever, the sedimentation rate is almost invariably elevated, but with clinical improvement of the patient there is a tendency for the rate to return to a normal level. Further, the sedimentation rate is higher in patients with severe symptoms than in those with moderate or mild symptoms, and during acute exacerbation of chronic disease there is an increase. Generally, clinical improvement is accompanied by significant improvement in the sedimentation rate.[37]

The sedimentation rate is usually elevated when a malignant tumor is present or when there is extension of the tumor through metastases.[38]

The sedimentation rate is likewise of value as a prognostic sign in the presence of known malignant tumors such as carcinoma of the breast or of the uterus. Patients who remain symptom free for long periods of time have a tendency to show normal sedimentation rates after adequate treatment of the primary lesion, but when the rate is consistently elevated or tends to rise in spite of therapy, metastasis and early death can be expected.[39] In general the same is true of Hodgkin's disease.[40] A general statement which can be made regarding malignancy is: "If a malignant growth is removed operatively the sedimentation rate should return to normal in six weeks if complete removal is accomplished. If the rate returns to normal and remains so for six months, a guardedly favorable prognosis may be given. If the rate becomes abnormal it indicates recurrence or metastasis."[40a]

31. **Fahraeus, R.**: Ueber die Ursachen der verminderten Suspensionstabilität der Blutkörperchen während der Schwangerschaft (Vorläufige Mitteilung), Biochem. Ztschr. **89:** 355-364, 1918.

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There are two recent modifications of the sedimentation procedure which can be carried out simply. When blood taken for a sedimentation rate is allowed to stand twenty-four hours before the test is made, the rate tends to decrease. Recently it has been stated that in cases of malignant tumors or Hodgkin's disease the twenty-four hour sedimentation rate tends to be maintained or perhaps increased.[41] This technic of performing a sedimentation rate immediately and again at the end of twenty-four hours with the same sample of blood has been advocated as a differential procedure for the diagnosis of malignant tumors. It has been accepted by some observers [42] and not by others.[43]

This second modification is that in which the blood obtained by pricking the finger is placed on a glass slide. The blood is allowed to dry. Normally it will form a dark agglutinated central mass and lighter peripheral rings. The blood of patients with cancer will produce a dotted curtain pattern with the peripheral rings absent and no visible central agglutinated mass.[44] Microscopically, the dried blood from patients with carcinoma has numerous triasteroid spicules scattered throughout.[44a]

In summary then, one may say that an elevated sedimentation rate is almost always indicative of some disease or of pregnancy. In general, patients with malignant lesions tend to have much higher sedimentation rates than do those with inflammatory lesions. Elevated rates due to inflammation when continued over a period of time or when further rises occur indicate a spread or increase in severity of the lesion. When the elevated rate is due to a malignant tumor, a continued elevation would suggest recurrence or metastasis, or both, and can be regarded as a bad prognostic sign. The subsidence of the sedimentation rate to a normal level in an inflammatory state generally indicates improvement, and in malignant lesions one can possibly give a guardedly favorable prognosis. The modifications of the procedure for sedimentation test which I have outlined must be investigated more thoroughly before they can be fully accepted as valuable adjuncts in diagnosis and in prognosis.

SUMMARY

From the vast number of laboratory tests available I have outlined some of the more useful ones which can be employed as regular office procedures. These tests have been selected for their simplicity and their value as indicators in diagnosis and in progress of disease. The indications for their use and the underlying principles are included.

The value of these tests depends largely on the care and accuracy with which they are done, and they should be conducted by the physician or by a well qualified technician, never by an unskilled, partly trained person.

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RESULTS OF RAPID TREATMENT OF EARLY SYPHILIS

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The participation of the U. S. Public Health Service in the evaluation of various treatment methods for early syphilis may be grouped in three broad phases. The first was the evaluation with the Cooperative Clinical Group of the results of standard therapy of weekly injections of arsphenamine and heavy metal. This study was conducted in the period 1930-1935. The second was the field study evaluation of massive arsenotherapy conducted with the New York and Midwestern groups of cooperating clinics that took place during the ten year period 1933-1943.

The present communication is a progress report on an evaluation study of the results in early syphilis of various intensive treatment schedules utilizing penicillin alone or with adjunctive therapy and of certain methods and schedules of intensive arsenotherapy. The records on which the study is based are from sixteen rapid treatment centers. These centers are members of a group of some fifty publicly supported hospitals which were established early in the war to permit large scale application of rapid treatment methods. The establishment of these facilities grew out of the observation that 75 per cent of patients with early syphilis admitted to clinics for routine therapy lapsed from treatment before receiving the minimum protective regimen of twenty arsenical injections together with heavy metals.

Schedules being studied in our current evaluation and reported on herewith are as follows:

METHODS OF TREATMENT EVALUATED

1. 300,000 units of penicillin (5,000 every three hours for eight days) with 320 mg. of arsenoxide but no bismuth.

2. 600,000 units of penicillin (10,000 every three hours for eight days) with no conjunctive drugs.

3. 1,200,000 units of penicillin (20,000 every three hours for eight days, 40,000 every six hours for eight days or 40,000 every three hours for four days) with no conjunctive drugs.

4. 1,200,000 units of penicillin (20,000 every three hours for eight days) with 320 mg. of arsenoxide but no bismuth.

5. 600,000 units of penicillin (10,000 every three hours for eight days) with 7 to 9 mg. of arsenoxide per kilogram of body weight and 600 mg. of a bismuth compound or 8-6-3 routine.

6. 1,200,000 units of penicillin (16,667 every three hours for nine days) with 4 to 6 mg. of arsenoxide per kilogram of body weight and no bismuth, or 5-12-0 routine.

7. 1,200,000 units of penicillin (16,667 every three hours for nine days) with 4 to 6 mg. of arsenoxide per kilogram of body weight and 600 mg. of bismuth, or 5-12-3 routine.

8. 2,400,000 units of penicillin (40,000 every three hours for eight days or 80,000 every three hours for four days) with no conjunctive drugs.

9. Multiple injection eleven to twenty days; 1,200 or more mg. of arsenoxide plus varying quantities of a bismuth compound.

10. Five day intravenous drip; 1,200 mg. of arsenoxide.

11. Eight day intravenous drip; 1,080 to 1,200 mg. of arsenoxide and twelve injections of a bismuth compound.

Read before the Section on Preventive and Industrial Medicine and Public Health at the Ninety-Fifth Annual Session of the American Medical Association, San Francisco, July 3, 1946.

V 13
1946

The present progress report shows the results obtained after twelve to fifteen months' observation in the treatment of approximately eight thousand rapid treatment center patients. To insure minimum observation only those patients treated prior to April 1, 1945 are included in this presentation with the exception of patients receiving 1,200,000 units of penicillin plus five injections of arsenoxide with or without the addition of three injections of a bismuth compound. This schedule was instituted so recently that patients treated through Dec. 31, 1945 but after April 1, 1945 had to be included in order to present preliminary results.

Records from sixteen rapid treatment centers utilized in the preparation of this report have been divided into two groups, A and B, to afford a more accurate presentation of results.[1] Group A facilities had more complete follow-up observation than those in group B. Only a relatively small proportion of the patients treated at group A centers were lost from observation by the end of one year. In addition, posttreatment examinations were performed on most of their patients at the center.

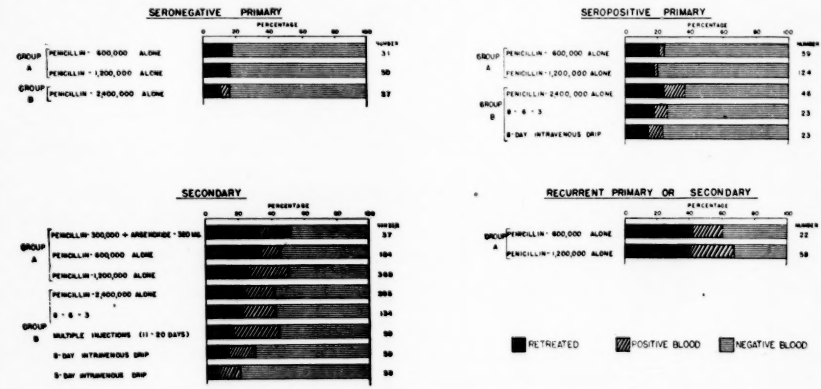

Chart 1.—Status of patients observed twelve to fifteen months after treatment by method of therapy, group A and group B facilities.

At group B facilities the serologic quantitative titer was relied on to a great extent for detecting "treatment failures."

In this report only those methods of treatment are included which have a minimum number of 20 cases in any specific diagnostic group or observation period.

COMPARATIVE RESULTS TWELVE TO FIFTEEN MONTHS AFTER TREATMENT

Chart 1 shows the status of cases observed twelve to fifteen months after treatment by admission diagnosis and type of treatment. Since only in the secondary syphilis group here studied were there sufficient cases observed twelve to fifteen months by all treatment methods, this group was used as the basis for comparing treatment methods.

In the treatment of secondary syphilis, five day arsenical intravenous drip was superior to the other six technics compared at the end of fifteen months. The percentage of cases exhibiting unsatisfactory results following the use of penicillin varied from 41 following 2,400,000 units of penicillin alone to 51 following 300,000 units plus 320 mg. of arsenoxide. The eight day schedule employing arsenoxide and bismuth in combination with 600,000 units of penicillin showed approximately the same percentage of satisfactory results as 2,400,000 units of penicillin alone, 58 per cent and 59 per cent respectively.

The last section of the chart shows the results of treatment of patients admitted as failures to an initial rapid treatment routine. It is interesting to note that from 15 to 17 per cent more patients exhibited an unsatisfactory response when treated for recurrent primary or secondary syphilis than for previously untreated secondary syphilis patients treated with the same schedules.

COMPARATIVE RATES SHOWING PERCENTAGE OF PATIENTS RETREATED

Chart 2 shows the cumulative percentage of patients with the admission diagnosis of previously untreated secondary syphilis who were retreated following clinical or serologic relapse, for reinfection or for seroresistance by treatment schedules employed at group A and group B facilities.

At group A facilities, 1,200,000 units of penicillin plus 320 mg. of arsenoxide showed the best results at the end of twelve months. However, the difference between this schedule and that employing 1,200,000 units of penicillin alone was not statistically significant. For penicillin alone, 1,200,000 units showed significantly better results than 600,000 units from the ninth through fifteenth months. The number of patients retreated between twelve and fifteen months is to a large extent composed of patients who had been showing unsatisfactory progress in the reduction of the quantitative titer reading and at the end of one year were routinely retreated.

It is interesting that, through the eighth month, 300,000 units of penicillin plus 320 mg. of arsenoxide showed a relatively low percentage of failures. By the fifteenth month, however, this schedule had a retreated rate of over 30 per cent. This trend is probably due to relapses being delayed by the addition of arsenoxide to the penicillin schedule. From this experience it can be

1. Group A, Chicago, Cleveland and New York. Group B, Norfolk, Durham, Charlotte, Augusta, Savannah, Jacksonville, South Charleston, Ann Arbor, Hot Springs, St. Louis, Memphis, Nashville and Chattanooga.

seen that the effectiveness of any method of treatment as judged by results during the first six months of follow-up may not be borne out by its effectiveness after twelve or fifteen months of observation.

In group B facilities, at the end of fifteen months significantly fewer patients were retreated following five day intravenous drip (5.0 per cent) than following 2,400,000 units of penicillin, 600,000 units of penicillin combined with eight arsenoxide and three bismuth injections (8-6-3) or multiple injection over eleven to twenty days (23, 22 and 16 per cent respectively). As will be shown in a later table, the fatality rate from five day intravenous drip was 1 per 149 patients treated. With the advent of penicillin, five day intravenous drip was discontinued in favor of the less toxic penicillin treatment. Among the treatment technics utilizing penicillin, very little difference was noted at the end of fifteen months in the percentage of failures between 2,400,000 units of penicillin (23) and 8-6-3 (22).

The two more recent treatment schedules employing 1,200,000 units of penicillin plus five injections of arsenoxide, one with three injections of bismuth (5-12-3) the other without bismuth (5-12-0) shown in this chart have had only ten to eleven months follow-up. With only 8 per cent failures 5-12-3 was significantly better than 5-12-0 (13 per cent failures) in the percentage of patients retreated by the tenth month. It would appear that the addition of 600 mg. of bismuth to the 5-12-0 routine resulted in a significant difference in the number of patients with secondary syphilis retreated. However, until patients treated by these two methods have had follow-up observation for a longer period of time, it cannot be determined whether the bismuth increased the success rate or delayed the occurrence of treatment failures.

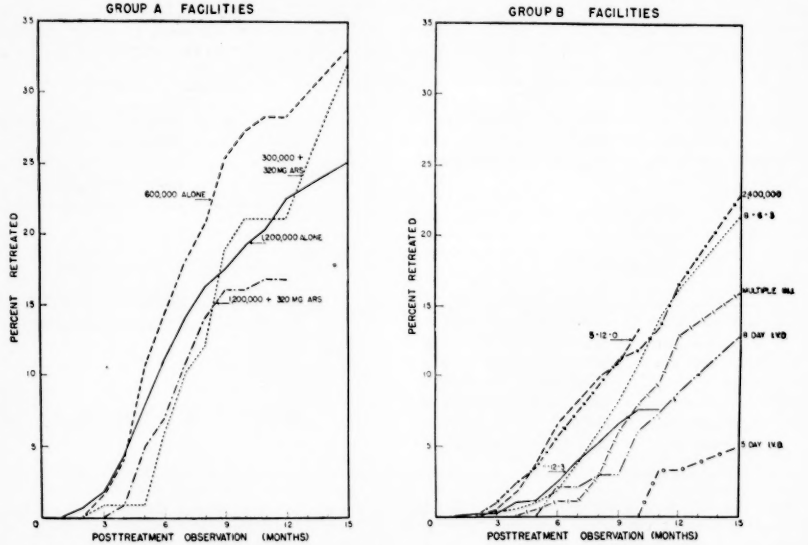

Chart 2.—Cumulative percentage of previously untreated secondary syphilis retreated for clinical or serologic relapse, seroresistance or reinfection.

EFFECT OF PENICILLIN DOSAGE PER INJECTION AND INTERVAL BETWEEN INJECTION ON NUMBER OF PATIENTS RETREATED

Chart 3 shows the number of patients retreated after 1,200,000 units of penicillin by the number of Oxford units per injection and the interval between injections. At the end of nine months there were significantly more patients retreated after the routine of 20,000 units of penicillin every three hours for eight days than under either the routine of 40,000 units every three hours for four days or the routine of 40,000 units every six hours for eight days. Although this significance did not carry over into the twelfth month period, it must be pointed out that only a small proportion of the patients given the 20,000 unit per injection routine have had the opportunity to be observed as long as twelve months following treatment. There is practically no difference at any observation interval in the results obtained by the administration of 40,000 units every three hours for four days when compared with 40,000 units every six hours for eight days.

CLASSIFICATION OF FAILURES AND VARIATIONS BY TREATMENT DIAGNOSIS

Of the 1,058 patients retreated as "failures" after having completed any rapid therapy routine, 67 per cent were retreated on the basis of clinical relapse. The remaining 33 per cent were retreated for the following reasons: 8 per cent for probable reinfection, 8.7 per cent for serologic relapse (negative to positive), 11.2 per cent for increased titer and 5.6 per cent for seroresistance. Because of differing classifications of treatment failures, timing for retreatment and employment of different schedules of therapy among rapid treatment centers, it was felt that comparisons of types of failures

V 13
1946

by various methods of treatment could not be made. Moreover, those centers with the best follow-up are apt to discover failures sooner, on the basis of serologic reactions, and thus have the opportunity to initiate retreatment before clinical evidence appears. Group A facilities retreated a significantly greater proportion of

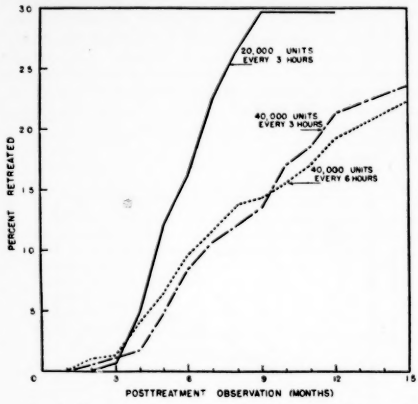

Chart 3.—Cumulative percentage of patients retreated following various time-dosage schedules of 1,200,000 units of penicillin for secondary syphilis.

patients on the basis of increased titer than the thirteen rapid treatment centers included in group B.

Chart 4 shows by admission diagnosis the cumulative percentage of total patients retreated, with breakdowns showing the percentage retreated for clinical relapse and the percentage retreated for probable reinfection. Only patients from group A facilities treated prior to Jan. 1, 1945 were included in the preparation of this chart. All methods of treatment at group A facilities were included in the compilations.

Chart 4 *A* shows that fifteen months following rapid therapy significantly more patients were retreated among those who had a diagnosis of recurrent primary or secondary syphilis at admission than among the previously untreated seronegative primary, seropositive primary or secondary syphilis patients. Further, significantly more patients were retreated among the secondary syphilis group than among the seropositive or seronegative primary syphilis patients. In observing the results at fifteen months it is apparent that the earlier treatment is begun the better the chances against relapse. A higher reinfection rate among seronegative primary cases explains the greater proportion in this group retreated between the third and seventh months as compared to the seropositive primary or secondary syphilis cases.

Chart 4 *B* shows that retreatment for clinical relapse follows the same general trends established in chart 4 *A* for the total group. The seronegative primary cases retreated, however, do not show as decided a rise during the first six months as was observed in chart 4 *A*.

It would appear from chart 4 *C* that, the earlier the stage of syphilis diagnosed at the time of treatment, the greater the chance of reinfection. The significant difference between primary and secondary syphilis in the proportion of probable reinfections reported is explained in part by the ability of the clinician to consider the site of the original lesion in determining whether the case involved is to be classified as a clinical relapse or a reinfection. There are three possible explanations for the significant difference between seronegative and seropositive primary syphilis. These theories are as follows: 1. Immunity. Presumedly cases treated in the earlier stages are more susceptible to reinfection. 2. Definition. By definition a reinfection can be determined only if the treated patient has become seronegative. 3. Reinfection by wife, paramour or other person who has remained untreated and infectious. This last possibility suggests the need for more effective contact investigation and better instruction of patients, including a discussion of the danger of reinfection by partners.

REACTIONS TO TREATMENT

The table shows the number of severe reactions and deaths by method of therapy among cases treated through March 15, 1945.

It will be noted that the reaction rate in schedules employing penicillin alone or in combination with small amounts of arsenoxide and bismuth is significantly less than in schedules utilizing arsenoxide as the principal drug. Of the schedules not using penicillin, multiple injection schedules had significantly fewer reactions than the intravenous drip technic.

There were no deaths in treatment schedules employing penicillin alone. Where penicillin was combined with eight injections of arsenoxide and three injections of bismuth there was one death per 4,312 cases treated. The death rate was considerably higher under the arsenoxide routines, where one death occurred for every 149 cases treated with five day intravenous drip, one per 1,238 cases treated with eight day intravenous drip and 1 per 1,873 patients treated by multiple injection.

Comparison of Schedules of Therapy for Syphilis Used in Rapid Treatment Centers in Terms of Severe Reactions and Deaths Through March 15, 1945

Schedules of Therapy	Total Cases	Patients with Severe Reactions: Number	Patients with Severe Reactions: Rate per 1,000	Deaths: Number	Deaths: Rate per 1,000
Penicillin alone	3,569	9	2.52	—	0.00
Penicillin-mapharsen-bismuth (8-6-3)	17,249	153	8.87	4	0.23
Five day intravenous drip	1,041	78	74.93	7	6.72
Eight day intravenous drip	3,713	256	68.95	3	0.81
Multiple injection, 11-20 days	1,873	77	41.11	1	0.53

SUMMARY AND CONCLUSIONS

1. Observation of approximately 8,000 patients treated in rapid treatment centers has led to a progress report on the results, based for the most part on twelve to fifteen months' observation, of the treatment of early syphilis by various intensive methods employing penicillin alone and with adjunctive drugs, in varying dosages and treatment intervals.

2. Wide variation was noted in the effectiveness of treatment begun in the various stages of early syphilis. Treatment begun in the primary stage gave considerably better results than that begun in the secondary stage or after relapse from a previous course of intensive therapy.

3. The study shows in the series of patients given fifteen months' posttreatment observation that there was no significant difference between the schedules evaluated using penicillin alone and those in which penicillin in smaller doses was administered with adjunctive arsenoxides.

4. There was no essential difference between the results observed in the use of 600,000 units of penicillin and schedules employing 1,200,000 or 2,400,000 units of penicillin alone. However, among a group of patients having a maximum observation period of ten months the 5-12-3 schedule gave better results at that observation point than the 5-12-0 schedule and better results than any other schedule employing penicillin. It would seem from this evidence that the effectiveness of any penicillin treatment method for early syphilis is probably enhanced by the inclusion of bismuth.

5. At the end of and throughout the observation period of twelve months there was no significant difference between the results obtained from 40,000 units of penicillin administered every three hours for four days and 40,000 units every six hours for eight days.

6. There were no deaths attributable to treatments using penicillin alone. When penicillin was combined with small amounts of arsenoxide and bismuth the mortality rate was one death in 4,312. With intensive arsenotherapy the mortality rate ranged from one per 149 cases in five day intravenous drip to one per 1,873 cases treated by multiple injection.

7. Because of the toxicity and relatively high mortality rate of massive arsenotherapy, such treatment methods were largely discontinued by rapid treatment centers participating in this study when preliminary evidence showed that considerable promise might be expected of schedules relying principally on penicillin. While the present study cannot be considered anything but preliminary, the wide availability of penicillin suggests that any form of intensive arsenotherapy should be used only with the utmost caution. Our present incomplete knowledge of final outcome of early syphilis treated with schedules relying principally on penicillin suggests that all patients so treated should be urged to return periodically for diagnostic check-up.

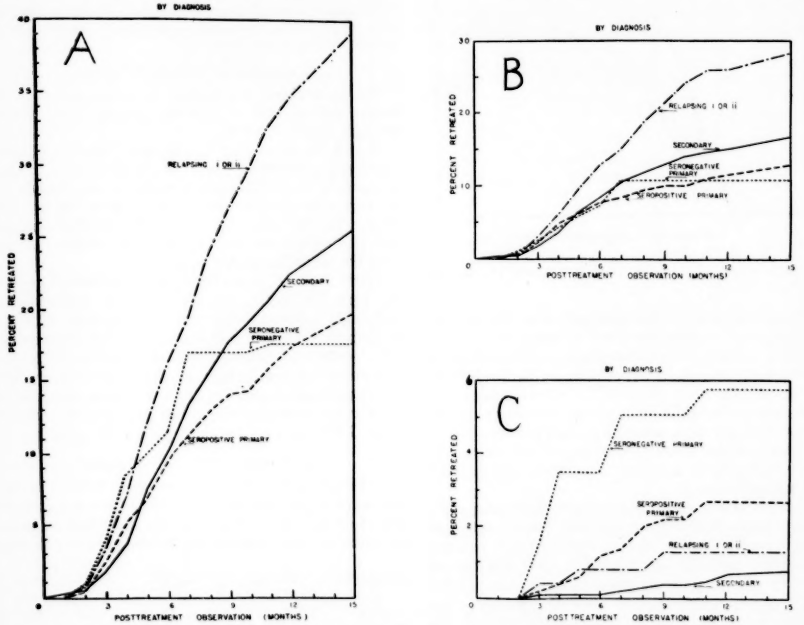

Chart 4.—*A*, cumulative percentage retreated for clinical or serologic relapse, seroresistance or reinfection. *B*, cumulative percentage retreated for clinical relapse. *C*, cumulative percentage retreated for probable reinfection.

ABSTRACT OF DISCUSSION

DR. BRUCE WEBSTER, New York: The penicillin treatment of early syphilis would appear to be in much the same status today as the arsenical therapy of this disease was in the period 1907 to 1910. I have recently seen an elderly Austrian with syphilitic aortitis who was given a single injection of arsphenamine by Ehrlich himself in 1909 and told that it could be expected to sterilize his blood stream and cure his disease. I was impressed with the increased percentage of cures that resulted when a relatively few doses of bismuth were added to the penicillin regimen. The same thing was observed when a bismuth compound was added to the five day intravenous drip and to the multiple injection method. It would seem likely that this increase in efficacy is due to the longer period over which bismuth acts, thus increasing the time over which a spirocheticidal agent is in continual action early in the disease. The eventual solution to the problem may be in a penicillin-bismuth

V 13
1946

combination or some newer method of prolonging the action of penicillin. Dr. Heller's data demonstrate strikingly the relatively poor prognosis in relapsing syphilis. The differentiation between relapses and reinfections is most difficult. Any method of rapid treatment seems to cut down the patient's immunity and increase the chances of reinfection. Relapses may be due to the development of resistant strains of Treponema pallidum, for which there is no evidence, or to the failure of development of host resistance, which seems more likely. Syphilis which relapses after any of the rapid treatment methods should be retreated, preferably by some more prolonged method. The overall result of penicillin therapy of early syphilis may be better than Dr. Heller's results indicate, because of the fact that his data cover a period when commercial penicillin contained a large amount of penicillin K. This penicillin K has been shown to be rapidly destroyed in the body and relatively nonefficacious against the spirochete. This has been corrected, and commercial penicillin now has a high percentage of penicillin G, which is destructive toward the spirochete. The question which I am sure every physician wants to ask is "Am I justified in using one of these experimental methods in the treatment of a patient with early syphilis who comes to my office?" I feel that any of the standard schemes for the use of penicillin in early syphilis now used by the Army or the Public Health Service is suitable for general use if the doctor is prepared to carry out an adequate follow-up for a minimum of two years. The use of these methods without such careful follow-up creates a serious menace both to the patient and to the community.

NITROGEN MUSTARD THERAPY

Studies on the Effect of Methyl-Bis (Beta-Chloroethyl) Amine Hydrochloride on Neoplastic Diseases and Allied Disorders of the Hemopoietic System

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and
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Chicago

The work of three groups of investigators on the therapeutic effects of the nitrogen mustards was recently summarized.[1] The first clinical application of these compounds was initiated by Gilman, Goodman and others,[2] who administered *tris* (β-chloroethyl) amine hydrochloride intravenously to a group of 6 patients in the terminal stages of a variety of neoplastic diseases. They observed a striking effect on hemopoietic tissue including the regression of lymphadenopathy in a case of lymphosarcoma. Independently in Chicago we initiated a clinical investigation of another nitrogen mustard, methyl-*bis* (β-choloroethyl) amine hydrochloride,[3] on patients with neoplastic diseases of the hemopoietic system on whom prolonged observation as to the therapeutic efficacy of the drug could be made.

From the Department of Medicine, the University of Chicago.

Part of the work described in this paper was done under contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the University of Chicago.

1. Rhoads, C. P.: Nitrogen Mustards in the Treatment of Neoplastic Disease, J. A. M. A. **131:** 656 (June 22) 1946.

2. Gilman, A.; Goodman, L.; Lindskog, G. E., and Dougherty, S.: This work at New Haven Hospital, Yale University, is referred to by Gilman and Philips.[4]

3. This investigation constitutes one of the three recently summarized.[1] Goodman, L. S.; Wintrobe, M. M.; Dameshek, W.; Goodman, M. J.; Gilman, A., and McLennan, M. T.: Clinical Experiences with the Use of Methylbis (β-Chloroethyl) Amine Hydrochloride and Tris (β-Chloroethyl) Amine Hydrochloride (Nitrogen Mustards) in the Therapy of Hodgkin's Disease, Lymphosarcoma, Leukemia and Certain Allied and Miscellaneous Disorders, J. A. M. A. **132:** 126 (Sept. 21) 1946, is the second study. The third is by Karnofsky, D. A.; Craver, L. F.; Rhoads, C. P., and Abels, J. C.: An Evaluation of Methyl-Bis (β-Chloroethyl) Amine Hydrochloride and Tris (β-Chloroethyl) Amine Hydrochloride (Nitrogen Mustards) in the Treatment of Lymphomas, Leukemia and Allied Diseases, to be published.

MATERIAL AND METHODS

The chemistry of this drug has been discussed in detail elsewhere.[4] When placed in aqueous solution it undergoes a series of transformation, of which the first transformation product, an ethylene-immonium derivative, is physiologically active. In this study the drug was administered at a daily dose of 0.1 mg. per kilogram of body weight. Patients were given courses of treatment varying from one to six consecutive daily injections. In the past two years we have largely confined the number of injections per course to four.

Ten milligrams of the drug previously placed in sterile tubes is dissolved in 10 cc. of sterile isotonic solution of sodium chloride. It is administered within five minutes of its preparation by injecting the amount desired into the rubber tubing of a Fenwal type intravenous medication set previously set up and delivering isotonic solution of sodium chloride to the patient at a relatively rapid rate. It is assured in this manner that the alkylamine is given prior to its transformation into the ethylene-immonium derivative. The rapid flow and dilution is sufficient to assure painless administration and to avoid subsequent phlebothrombosis.

The patients in whom the therapeutic effects of the drug were studied had a variety of neoplastic diseases of or involving the hemopoietic system. The number of patients studied and their respective diseases are given in table 1. The patients studied were regular admissions to the hematology clinic. No attempt was made to select the patients on the basis of the duration or status of the disease. For the first two years of the study all patients were routinely hospitalized for treatment for periods varying from two to eight weeks in order to facilitate exhaustive pretreatment and post-treatment studies of the toxic and therapeutic effects of the drug. In the past year only new patients and selected patients previously treated have been hospitalized for a course of treatment.

The clinical evaluation of each patient included a careful history, a study of the biopsies taken prior to admission to our clinic if available and the amount of and response to roentgen therapy. In the physical examination special attention was given to abnormal masses such as an enlarged spleen, liver or lymph nodes. All such abnormalities were recorded whenever possible by direct measurement. A lymph node biopsy was performed in all cases of Hodgkin's disease and lymphosarcoma prior to the initiation of therapy. Studies of the peripheral blood routinely included: hemoglobin in grams per hundred cubic centimeters; erythrocytes, leukocytes, platelets and reticulocytes per cubic millimeter, and a differential leukocyte count (Wright's stain). Sternal aspiration with a direct count of nucleated cells and differential counts on dry stained films were made in selected cases before and after treatment. As a rule urea clearance, plasma proteins, albumin and globulin ratio and cholesterol (total and esters) were determined for each patient before and after treatment. Roentgenographic studies of the chest were made on all patients, and those of skeletal areas were made if they seemed indicated by the patient's clinical history and examination. If there were gastrointestinal complaints or abdominal masses,

4. Gilman, A., and Philips, F. S.: The Biological Actions and Therapeutic Applications of the β-Chloroethyl Amines and Sulfides, Science **103:** 409, 1946.

films were made of these areas with contrast fluoroscopy. The basal metabolic rate was determined before and after treatment when feasible.

POST-TREATMENT OBSERVATION

During and after treatment the leukocyte count and differential counts were made every second day. The erythrocytes, hemoglobin and platelets were determined

TABLE 1.—*Diseases Treated with Methyl-Bis (Beta-Chloroethyl) Amine Hydrochloride and Summary of Results*

Diagnosis	No. of Cases	Follow-Up, Mo.	Remission Duration, Mo.	Living	Dead
Hodgkin's disease	27	3 to 33	1 to 8	19	8
Lymphosarcoma	6	3 to 24	0 to 18	4	2
Lymphatic leukemia	9				
Acute	1	1.5	0	0	1
Chronic	8	6 to 21	0 to 21	3	5
Myelogenous leukemia	8				
Acute	1	3	0	0	2
Chronic	7	1 to 18	0 to 12	3	4
Sympathoblastoma	2	5 to 16	0.5 to 2	0	2
Multiple myeloma	2	5	Less than 2	0	2
Polycythemia rubra	5	3 to 17	Over 12	5	0

twice a week for the first two weeks and once a week thereafter. If the leukocyte count fell below 2,000 per cubic millimeter it was repeated daily until an upward trend was apparent. All blood studies were continued for a period of at least two months after treatment. The patient was examined at least once a week; measurements and notes were made of the changes observed. In selected cases photographic or roentgenographic studies were made before treatment, on the fifteenth and thirtieth day after therapy and were repeated monthly as indicated. Post-treatment biopsies from lymph node and rib were made whenever possible. All the pretreatment studies which have been outlined were repeated before each course of injections if indicated.

RESULTS

A. *Toxic Manifestations.*—The toxic reactions which are seen in patients after the administration of methyl-*bis* (β-chloroethyl) amine hydrochloride in doses as described previously may be classified as (*a*) immediate and (*b*) delayed. The immediate reaction consists largely of nausea and vomiting, which usually ensue two to three hours after the administration and persist for three to four hours. The severity of the nausea and vomiting varies considerably from person to person. An occasional patient experiences no untoward symptoms. When injections are given daily over a period of four days, which is the usual procedure, most patients are reluctant to eat and consequently lose weight during this period. In several of the 59 cases studied, diarrhea developed during treatment.

The delayed toxic reactions which may ensue are local thrombosis and thrombophlebitis at the injection site and widespread destruction of hemopoietic tissue. The local venous complications are entirely avoided if the material is injected by the method described earlier and if the vein chosen for the injection is not partially obstructed by tumor tissue.

The effects of the drug on the hemopoietic system which are potentially the most serious may progress to a complete aplasia of the hemopoietic elements of the bone marrow and widespread destruction of lymphatic tissue. This we have shown by biopsy of material from the lymph node and rib and by sternal aspiration on selected patients after treatment. The hematologic constituents of the peripheral blood show a chronologic sequence of changes which parallel closely the observations in the bone marrow aspiration and in biopsy material. The changes observed in the constituents of the peripheral blood after a course of four daily injections are illustrated in figure 1.

The initial change is lymphocytopenia which usually becomes apparent within twenty-four hours after the first injection and is progressive for six to eight days. Occasional degenerating lymphocytes are seen in the peripheral blood during this period. These degenerative forms vary from increased clumping of nuclear chromatin to complete disintegration of the nucleus with "rounded up" chromatin clumps free in the cytoplasm. Many lymphocytes take a more basophilic cytoplasmic stain and many may have nucleoli, thus making differentiation from blastocytic forms difficult during the period of maximum lymphopenia. A rare macrophage with engulfed débris has also been observed in the stained smears of peripheral blood during this period. Lymphocytic values tend toward normal between the second and third weeks after the last injection in some cases, while in others they may be depressed for longer periods. The monocytes follow the same course. Atypical monocytes and lymphocyte–monocyte transition forms are common within the first week after the initial injection. The total leukocyte count declines progressively for fifteen to twenty-one days. This is due largely to a severe neutropenia. The duration of the neutropenia is relatively short, and recovery is usually complete within two weeks after the maximum reduction. Recovery from the neutropenia may be

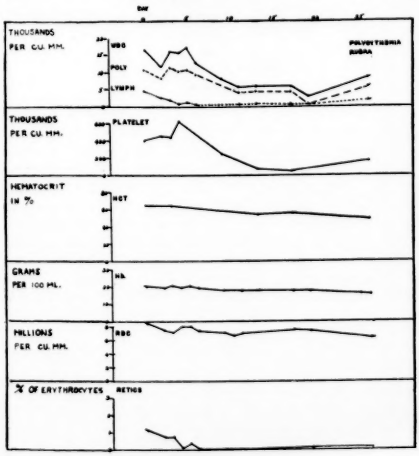

Fig. 1 (case 41).—Acute effect of four daily injections of methyl-*bis* (β-chloroethyl) amine hydrochloride on the hematologic constituents of the peripheral blood of a patient with polycythemia rubra.

heralded by a monocytosis. The neutrophils may also show morphologic changes indicating disintegration during the period in which neutropenia is developing. Myelocytes and metamyelocytes as well as giant forms of the mature and immature cells of the granular series are seen as early as the first week. With the onset

V 13
1946

of recovery a decided shift to the left in the granular series appears in the peripheral blood of most patients.

During the third week after a course of treatment, there is a variable tendency to a thrombocytopenia. Platelet counts have been observed to fall to 20,000 per cubic millimeter but usually range between 60,000 and 100,000. The reduction in platelet values is sufficient at times to produce a prolonged bleeding and delayed clot retraction time, but no significant changes have been found in the prothrombin values or clotting time. Purpura has appeared after treatment on one occasion in each of 4 patients, in whom petechial hemorrhages occurred over the buccal surfaces and over the legs below the knees.

A decline in the erythrocyte and hemoglobin values occurs in the first two weeks after treatment. The decline is roughly proportional to the dose of the drug but usually is not greater than 1 Gm. per cubic centimeter of hemoglobin and 300,000 erythrocytes per cubic millimeter. In the fifth week there is a slight tendency to macrocytosis during the period of active regeneration in the bone marrow. Studies on the total urobilinogen excretion in selected patients indicate a definite increase in erythrocyte hemolysis after treatment with methyl-*bis* (β-chloroethyl) amine hydrochloride. The reduction in hemoglobin and erythrocytes observed after the treatment of patients with polycythemia rubra is much greater than that which occurs in patients with the other diseases studied, such as Hodgkin's disease and lymphosarcoma.

Reticulocytic values decline within the first week after the initial injection. The degree of decline is obviously dependent on the dose per injection and the number of injections per course, but a course of four injections is invariably followed by a decline to less than 0.1 per cent. This decline is concomitant with the reduction in the erythrocyte precursors observed in bone marrow aspiration material. Evidence of regeneration is seen occasionally in the second and third week after injection, but normal values are not reached until the fourth or fifth week. It is common to find values above the normal range in the second and third month, after a course of treatment. This phase of regeneration is preceded by evidence of regeneration in the bone marrow.

It is worthy of note that only 1 infection has occurred in the patients studied in spite of the numerous leukopenias which have developed. The infection, an erysipelas of the face, occurred in a person with far advanced Hodgkin's disease whose leukocytes had fallen to 800 per cubic millimeter fifteen days after treatment with the drug. This patient had a history of recurrent erysipelas of the face before treatment was initiated. The infection was controlled effectively with penicillin therapy.

Recovery from the leukopenias produced by this drug is not influenced favorably or unfavorably by the administration of adequate therapeutic amounts of pentnucleotide, ferrous adenylate, leukocytic extract or folic acid, nor do whole blood transfusions appear to alter the spontaneous recovery observed in all patients.

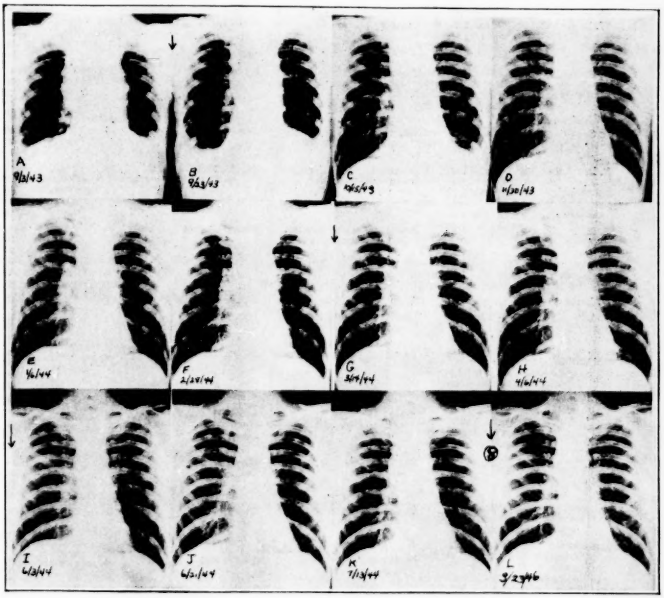

Fig. 2. (case 2).—Roentgenograms showing effect of therapy on the progress of the mediastinal and hilar lesion; *A* through *L* represent the pretreatment and subsequent films taken during the period of observation. The arrow inserted between reproductions indicates that a treatment was given; from July 13, 1944 to March 1946 (*K* and *L*) eight courses of the drug were administered.

The many miscellaneous clinical laboratory tests which were performed on selected patients and which included urea clearance, cholesterol and cholesteral esters and plasma protein determinations were not affected by a course of treatment. In fact, patients with definite damage to the liver and kidney were treated with repeated courses of the drug without untoward effect on the measurable function of these organs.

B. *Therapeutic Effects.* — Hodgkin's Disease: In a group of 27 cases of Hodgkin's disease the patients have been observed after treatment with methyl-*bis* (β-chloroethyl) amine hydrochloride for from three to

thirty-three months. Table 2 summarizes briefly the pertinent data on each patient. In these patients remissions have been produced varying from zero to eight months in duration. Of the original 27 patients, 8 have died from an extension of the disease as the drug or roentgen therapy or both failed to produce further remission.

As is apparent in table 2 several patients have been treated with the drug who were classified as resistant lymph nodes, but the patient expired. Case 16 has been followed for twenty-five months since treatment with the drug was initiated, and the patient continues to show a satisfactory response to each course of treatment. In case 20, a patient whose disease was of five years' duration and no longer responded to roentgen ray therapy has been under observation for nineteen months. Each of four courses of treatment with the drug have induced a remission averaging four to five

TABLE 2.—*Résumé of Cases of Hodgkin's Disease Treated with Methyl-Bis (Beta-Chloroethyl) Amine Hydrochloride*

Case	Patient	Age	Sex	Onset of Disease	Previous Therapy and Results	Courses of Treatment: Date of First	Courses of Treatment: No. Given	Period of Observation in Mo.	Average Duration of Remissions in Mo.	Comment
1	C. C.	23	M	March 1942	Roentgen ray, partial remission	May 27, 1943	10	27	2	Definite improvement with each course of treatment enabled patient to continue working, but remissions become shorter; roentgen ray not effective; died August 1945
2	W. D. S.	36	M	Jan. 1942	None	Sept. 7, 1943	14	33	2½	Fever, peripheral lymphadenopathy and spectacular mediastinal enlargement resolved; maintained symptom free up to present
3	F. S.	19	M	Nov. 1942	Roentgen ray repeatedly with minimum effect	Nov. 23, 1943	6	11	1 to 2	Remarkable temporary relief of symptoms and resolution of peripheral lymph nodes, but disease progressed and remissions unsatisfactory; died 11/4/44
4	A. G.	32	M	Sept. 1940	Roentgen ray repeatedly with no further effect	Jan. 14, 1944	2	7	3+	Good therapeutic response with each treatment; no longer under observation
5	F. D.	19	M	April 1942	Roentgen ray with remission of 6 to 7 mo.	Dec. 29, 1944	9	18	3 to 7 with 1st 3 treatments	Mediastinal enlargement has never recurred since 1st treatment; having prophylactic treatments with the drug every 2 mo.; no exacerbation yet apparent; able to work continuously
6	E. M.	31	F	Sept. 1941	Roentgen ray with remissions decreased to zero	March 17, 1944	6	18	1 to 3	Remarkable improvement after 1st course, patient able to return to work; roentgen ray attempted again without response; remissions with the drug progressively shorter; died 10/2/45
7	H. E. A.	58	F	June 1943	None	Jan. 7, 1944	2	5	3½	Left city; no further report obtained
8	T. L.	45	F	March 1943	Roentgen ray with remissions of about 1 mo.	Dec. 29, 1944	9	18	2 to 3	Lymphadenopathy and secondary edema of lower extremities responded to each course of therapy
9	J. M. B.	26	..	Nov. 1944	Roentgen ray, no response	Jan. 5, 1945	3	5	1 to 2	Cough, pruritus, lymphadenopathy improved with each treatment but lung lesions progressed and patient died; roentgen ray therapy attempted in month before death without effect
10	J. R.	17	M	1944	None	April 6, 1945 combined with x-ray	2	14	7	Peripheral lymphadenopathy and parenchymal lesions of lungs have responded well to the drug combined with roentgen ray
11	L. K.	28	F	1940	Roentgen ray; no longer responded	May 21, 1945	3	13	4 to 5	Weakness, weight loss, fever, lymphadenopathy, splenomegaly and hepatomegaly responded well to the drug and patient continued to work
12	P. H.	53	M	Oct. 1944	None	May 1, 1945	4	17	3 to 4	Fever, weakness, malaise, lymphadenopathy and splenomegaly disappeared after each course of therapy with the drug
13	D. K.	63	M	Dec. 1942	Roentgen ray, but no longer responded	May 9, 1945	1	2	0	Had been intensively treated with roentgen ray; no change after the drug except moderate reduction in size of lymph nodes; died 2 mo. after treatment
14	L. H.	35	F	Sept. 1944	None	Sept. 25, 1945	3	10	4	Fever, adenopathy, pleural effusion and mediastinal mass largely disappeared with each treatment; gained weight and able to return to work

to roentgen ray therapy; special attention should be directed to cases 4, 13, 16 and 20, which illustrate that in certain of these patients treatment with the nitrogen mustard produced significant remissions, while essentially no remission was induced in others. One patient (case 4) after receiving an initial course of the drug remained in a remission for three months, at which time a second course of treatment was given and another remission induced. He left the city four months after the second treatment, and we were unable to learn of his progress. In case 13 the patient was essentially moribund when treatment was instituted. The drug temporarily reduced the size of the peripheral months, and the patient is able to continue gainful employment. The therapeutic effect of methyl-*bis* (β-chloroethyl) amine hydrochloride in certain cases of Hodgkin's disease has been largely negligible. In these cases however, roentgen ray therapy was ineffective also. It is of great interest that certain patients will respond favorably to the drug when roentgenologic therapy has become of no value, while other patients who have become unresponsive to such therapy obtain no significant clinical remission.

The rapid resolution of the peripheral, intrathoracic and abdominal lymphadenopathy, the reduction in the size of the spleen and liver and the prompt alleviation

V 13 1946

of fever and malaise are often striking. Osseous pain and pruritus have responded favorably to treatment in a few cases. Recovery from moderate anemias has occurred in several cases with no other treatment than a course of the drug.

Case 2, which has been followed for a period of thirty-three months and in which the patient had repeated courses of the nitrogen mustard, is summarized here.

TABLE 2.—*Résumé of Cases of Hodgkin's Disease Treated with Methyl-Bis (Beta-Chloroethyl) Amine Hydrochloride —Continued*

Case	Patient	Age	Sex	Onset of Disease	Previous Therapy and Results	Courses of Treatment: Date of First	Courses of Treatment: No. Given	Period of Observation in Mo.	Average Duration of Remissions in Mo.	Comment
15	R. D.	33	M	Oct. 1941	Extensive treatment with roentgen ray	Dec. 19, 1945	1	2	0	Anorexia, malaise, lymphadenopathy and fever not influenced favorably with drug; died
16	F. G.	53	M	Jan. 1941	Repeated roentgen ray with last remission of only 1 mo.	May 17, 1944	6	25	4	Continued in good health with resolution of lymphadenopathy and symptoms after each treatment with the drug
17	G. M.	37	M	Dec. 1941	Repeated roentgen ray with decreasing lengths of remission	Nov. 1, 1943	5	13	6 to 7	Remission first induced of 7 mo. duration but thereafter of 1 mo.; roentgen ray therapy again attempted without effect; died Jan. 1, 1945
18	O. M.	40	M	Jan. 1943	Roentgen ray with remissions of 3 mo.	July 24, 1944	8	24	3 to 5	Fever, fatigue and lymphadenopathy disappeared with 1st course; thereafter recurrence of "fever" only indication for therapy; feels well and continues to work
19	J. C.	27	M	Nov. 1943	Roentgen ray with remissions of 3-4 mo.	Oct. 1, 1944	10	21	2 to 5	Initial malaise, fever and lymphadenopathy disappeared on treatment with the drug; no lymphadenopathy has recurred, only indications for treatment with drug are fever, anemia, leukopenia and thrombocytopenia
20	G. M.	45	F	Sept. 1938	No longer responded to roentgen ray or radioactive phosphorus	Dec. 23, 1944	4	19	4 to 5	Fever, malaise, lymphadenopathy and splenomegaly responded to 1st and subsequent courses of the drug
21	J. W.	27	M	Jan. 1943	Roentgen ray with remissions of 4-6 mo.	Feb. 22, 1945	4	16	4	Fever, weakness, malaise, lymphadenopathy, splenomegaly and hepatomegaly responds to each course of treatment with the drug
22	M. L.	36	M	June 1943	Roentgen ray with only partial and brief remission	Feb. 20, 1945	3	12	1 to 2	Severe pain in back and extremities, fever and generalized lymphadenopathy relieved for only about 1 mo. with each course of therapy; died January 1946
23	E. L.	21	M	June 1942	Extensive treatment with roentgen ray; response to last course unsatisfactory	Sept. 14, 1945..	6	10	1 to 3	Fever disappeared with each course of treatment; adenopathy and splenomegaly decreased; patient felt well and able to return to work
24	J. P.	17	M	1944	Repeated roentgen ray with no further response	Dec. 14, 1945	4	7	2+	Fever ended with therapy; large neck mass and general lymphadenopathy decreased; in much better general health
25	H. S.	28	M	1945	Roentgen ray with poor response	Dec. 29, 1945	1	7	7+	Fever ended with therapy; lymphadenopathy resolved; patient feeling well and continues to work
26	J. O.	25	F	June 1, 1943	Extensive treatment with roentgen ray, with no further effect	July 25, 1945	4	12	1+	Bone pain, pronounced weakness and fatigue, cough and fever which no longer responded to roentgen ray were favorably influenced by the drug for periods of at least a month for the 1st 3 courses; thereafter, no longer effective
27	E. W.	30	F	Jan. 1943	None	April 3, 1944	4	20	5	Began roentgen ray therapy in another city in January 1946

CASE 2.—W. S., a man aged 37, a commercial artist, was admitted to Billings Hospital on Aug. 24, 1943. About eighteen months prior to admission there developed enlarged, slightly tender cervical lymph nodes and, later, a nonproductive cough with increasing dyspnea. Four weeks before entering the hospital, dysphagia, pronounced hoarseness and pain in the right arm with radiation to the wrist developed.

On examination this patient was found to be a somewhat emaciated man with a temperature of 101 F. and a pulse rate of 100, and he was in great respiratory distress. A generalized nontender lymphadenopathy, increased mediastinal dulness on percussion and a liver and spleen palpable 6 cm. below the right and left midclavicular line, respectively, were the essential positive physical observations. Biopsy of a cervical lymph node revealed the classic histologic signs of Hodgkin's disease. A roentgenogram of the chest (fig. 2*A*) showed definite mediastinal involvement. A small amount of free fluid was present in both costophrenic angles.

Six daily intravenous doses of 5.4 mg. of Methyl-*bis* (β-chloroethyl) amine hydrochloride were given September 7 to 13 inclusive. Approximately three hours after each injection nausea and vomiting occurred and persisted for two to three hours. A leukopenia developed, which reached a minimum of 1,700 cells per cubic millimeter on the sixteenth day and slowly rose to 3,100 on the twenty-eighth day after the initial injection. On the day of the third injection the patient noticed improvement in breathing, and the cough, dysphagia and hoarseness had decreased. Within one week the cervical lymphadenopathy had decreased about one third in size. Daily fever up to 101 F. which was present on admission and throughout treatment disappeared three days after the completion of therapy.

A film of the chest (fig. 2*B*) sixteen days after the first injection showed a reduction of the mediastinal mass to one-half its former size. The small amount of fluid in the costophrenic angles had increased slightly.

One month after treatment the patient had gained 6 Kg. in weight and stated that his appetite and endurance were better than they had been for several years. The hoarseness, dysphagia and cough had disappeared. The nodes in the cervical, axillary and inguinal regions had resolved (figs. 3 and

4). The spleen and liver were not palpable. Roentgenograms of the chest (fig. 2*C* and 2*D*) showed a further decrease in the size of the mediastinal mass, and the fluid present in the right costophrenic angle had disappeared.

On Jan. 6, 1944, four months after treatment, he had no symptoms but lymph nodes in the right cervical region were again

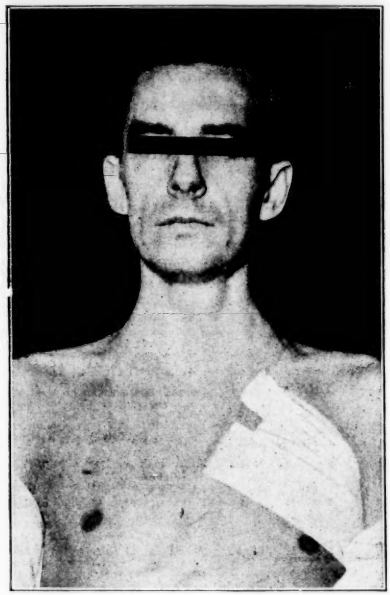

Fig. 3 (case 2).—Photograph of the neck area showing the gross enlargement of the supraclavicular and cervical nodes before treatment.

palpable. The nodes in other regions were not increased in size, and the spleen was not palpable. A roentgenogram of the chest on Jan. 6, 1944 (fig. 2*E*) showed that the principal mediastinal mass had not changed since Nov. 30, 1943; however, a new clump of enlarged glands had appeared in the hilus of the right lung. Five months after the first treatment the patient still felt well and body weight had been maintained, but lymph nodes in the neck, axilla and inguinal region had increased in size, and the spleen was palpable 3 cm. below the costal margin. He was admitted to the hospital. A film of the chest (fig. 2*F*) disclosed considerable increase in the mass at the right hilus. The intravenous injection of 6 mg. a day of the drug was started Feb. 28, 1944 and continued for six consecutive days. By March 14, 1946 the peripheral nodes and spleen were normal on palpation and the pleural lesions had improved (fig. 2*G*). A subsequent film taken on April 6, 1944 revealed a relatively normal chest (fig. 2*H*).

In view of the success in producing remissions with the nitrogen mustard in this patient, it seemed desirable to investigate the therapeutic effect of more frequent injections. It was decided to give two injections of the same dosage (0.1 mg. per kilogram) every six to eight weeks. On May 24 and 25, 6.1 mg. of the drug were given intravenously on each of the two consecutive days. One month later, however, a roentgenogram of the chest (fig. 2*I*) showed a slight increase in the size of the mediastinal nodes. There were no other signs of activity. This suggested that two daily injections of the drug were not sufficient to produce an adequate remission.

A progressive growth of the mass in the superior mediastinum was observed on the film of July 13, 1944 (fig. 2*K*). The patient however, remained symptom free.

On July 15 to 17, inclusive, the patient received three daily injections of 6.1 mg. of the drug. The immediate toxic reactions were mild, but the usual leukopenia occurred. A roentgenogram on July 27, twelve days after treatment, showed regression of the mediastinal shadow. This trend continued for two months, and it was not until August 24 that a definite reactivation of the mediastinal nodes was observed.

Since September 1944, eight more courses of the drug have been given, the last from March 5 to 7, 1946. The material was administered every twelve hours instead of once every twenty-four hours during each course, as described above. Nausea, vomiting and leukopenia have followed each course as has regression of peripheral or intrathoracic lymph nodes. A film of the chest taken in March 1946 is shown in figure 2*L*.

It is worthy of note that while this patient has now had an active type of Hodgkin's disease for more than four years, it has been controlled for thirty-three months without an apparent decline in the health of the patient or change in his response to the drug. Except for the brief periods of hospitalization for treatment, he has worked continuously. The indication for treatment has been the appearance or enlargement of the lymph nodes. He has had no symptoms referable to his disease since the first treatment with the drug.

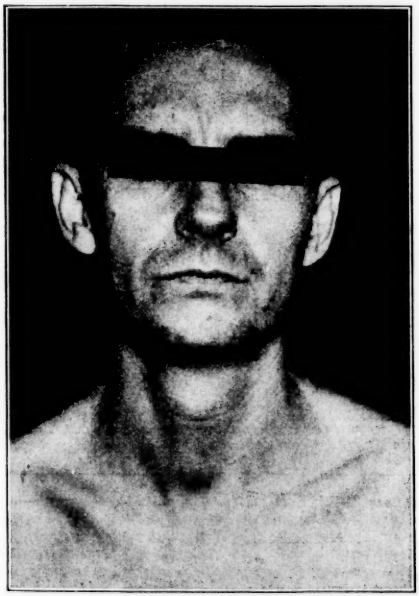

Fig. 4 (case 2).—Photograph of the neck area showing complete resolution of the nodes ten days after treatment.

Lymphosarcoma: Six patients with lymphosarcoma have been treated with methyl-*bis* (β-chloroethyl) amine hydrochloride. The pertinent data on each case are summarized in table 3. In 4 of the 6 patients clinically significant remissions were produced, varying

V 13
1946

from three to eighteen months in duration. Repeated courses of the drug have effectively produced further remissions essentially similar to the initial response in these 4 patients, and they continue under observation. Two patients (cases 29 and 30) were in a terminal state on arrival at the hospital, and death in each case

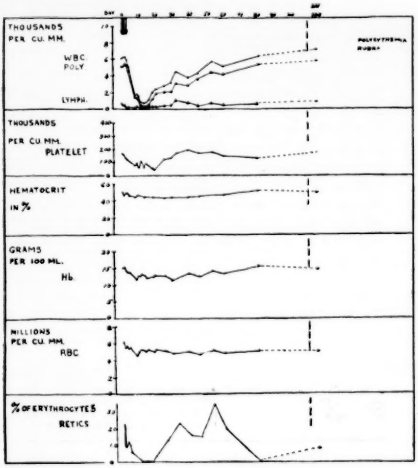

Fig. 5 (case 43).—Effect of four daily injections of methyl-*bis* (β-chloroethyl) amine hydrochloride on the hematologic constituents of the peripheral blood of a patient with polycythemia rubra over a period of six months.

resulted from a widespread invasion of an extremely undifferentiated tumor. Only a temporary and relatively insignificant clinical improvement resulted from a course of the drug in these 2 latter cases.

Lymphatic Leukemia: Nine cases of lymphatic leukemia have been treated with the drug. Eight were of the chronic variety and are summarized in table 4. In 1 case of acute lymphatic leukemia, an eighteen year old boy was given 5.5 mg. of the drug intravenously on two consecutive days. This treatment failed to alter the progress of the disease, and the patient died six weeks after the initiation of methyl-*bis* (β-chloroethyl) amine hydrochloride therapy.

Although all the patients with chronic lymphatic leukemia except 1 responded to the initial course of the drug with remissions which lasted from two to twenty-one months, 5 of them died after a year or more of observation from extension or complications of the primary disease process. One patient (case 39) continues in remission twenty-one months after a course of treatment with the drug and another (case 37) has obtained remissions of six and twelve months, respectively. The patient (case 40) who failed to respond adequately to the drug has responded favorably to treatment with parenterally administered radioactive phosphorus.

Myelogenous Leukemia: Seven patients with chronic and 1 with acute myelogenous leukemia have been treated with methyl-*bis* (β-chloroethyl) amine hydrochloride. Except for a transitory symptomatic improvement and a reduction in the leukocytes of the peripheral blood, results have been generally unsatisfactory in all but 3 patients. Roentgen ray therapy was reinstituted in those patients unresponsive to the drug with largely unsatisfactory results also. Three of the 7 patients with chronic myelogenous leukemia are receiving courses of the nitrogen mustard with repeated remissions of six and twelve months.

In 1 case of acute myelogenous leukemia, the patient who was given a standard course of treatment with the drug failed to respond favorably and expired within three months of the initial injection.

Sympathoblastoma: Two patients with sympathoblastoma were given courses of methyl-*bis* (β-chloroethyl) amine hydrochloride. Both had large tumor masses in the abdomen and metastasis to the neck when first seen. The tumor arose in the region of the right adrenal in 1 patient and from malignant degeneration of a neuroma of the abdominal sympathetic chain on the right side in the second. This tumor is characterized by its rapid extension to the lymph nodes, liver, skull, ribs and long bones with a rapidly fatal course. In each case the drug produced a rapid decrease in the size of the tumor masses and although short remissions followed, the general condition of both patients improved after their first, second and fifth courses. The total duration of their disease after diagnosis was ten and sixteen months respectively, which compares well with that for patients treated by roentgen therapy.

It is of interest that these undifferentiated tumors of nervous origin respond to the drug and suggests that its physiologic effect may depend on a reaction common to all rapidly proliferating cells. The remissions produced were short and serve as an index of the malignancy of the tumor. An evaluation of the efficacy of the drug in controlling sympathoblastoma is impossible from this limited experience.

Multiple Myeloma: Two patients with plasma cell myeloma were given courses of methyl-*bis* (β-chloroethyl) amine hydrochloride. One of them obtained some relief from pain in the back and in bones and in general was more comfortable for four months after treatment but died at home in the fifth month after treatment. Similarly, the other patients who had lesions in the vertebral column with a complicating Brown-Séquard syndrome had moderate relief of osseous pain for three to four weeks after a course of the drug, but no other improvement was observed. The reaction of the peripheral blood in each case was similar to that described previously. Studies of sternal aspiration material were made before treatment and at three day intervals after treatment. There was only a slight decrease in the total nucleated cell count. The tumor cells were not reduced in number nor were morphologic changes seen in the myeloma cells attributable to the treatment. Rib biopsies were made, in 1 case, before treatment and one week after treatment. Study of colloidin-embedded, hematoxylin, eosin and azure-stained sections of this material showed no evidence of regression of the nests of plasma cells or of morphologic change in the individual tumor cells.

Polycythemia Rubra: The effects of methyl-*bis* (β-chloroethyl) amine hydrochloride on the erythropoietic tissue suggested its use in polycythemia rubra. Five cases are now under observation, in each of which the patient has received a course of four injections.

These cases are summarized in table 5. In case 41 the patient has been observed for a period of seventeen months since the initiation of treatment with the drug. The patient in case 43 had remissions of six months on two occasions after treatment with radioactive phosphorus. After one course of the nitrogen mustard a symptomatic and hematologic remission was induced which still persists six months after treatment. Figure 5 illustrates the initial acute effect and the subsequent effect of treatment with the drug on the hematologic status of the peripheral blood of this patient. Definite symptomatic and hematologic remissions were produced in the 3 other patients with erythremia who were given a course of treatment with the drug, and the remissions continue after three to four months of observation.

TABLE 3.—*Résumé of Cases of Lymphosarcoma Treated with Methyl-Bis (Beta-Chloroethyl) Amine Hydrochloride*

Case	Patient	Age	Sex	Onset of Disease	Previous Therapy and Results	Courses of Treatment: Date of First	Courses of Treatment: No. Given	Period of Observation in Mo.	Average Duration of Remissions in Mo.	Comment
27	P. V.	24	F	1943	None	April 1944	4	28	1 to 4	Peripheral lymphadenopathy and abdominal mass disappeared as did weakness and fatigue; continues to feel well and is working
28	E. G.	30	M	March 1943	None	June 1944	4	24	4 to 7	Fever and malaise disappeared; adenopathy resolved; has gained weight and continues to feel well; treatment repeated because of reappearance of peripheral nodes
29	B. D.	37	F	1944	Extensive roentgen ray therapy with no results	May 1944	1	3	2	Decrease in size of enormous neck mass and some general improvement in symptoms therefrom; died August 1944 of phlegmonous infection of neck unrelated to therapy
30	R. S.	35	M	1942	Extensive roentgen ray therapy with initial remission but no further response	March 1943	1	3	0	No response in a rapidly growing reticular cell type lymphosarcoma; died 6/9/45
31	M. K.	38	M	July 1943	None	October 1943	4	33	2 to 18	Malaise, weakness and fatigue disappeared and peripheral lymphadenopathy resolved; continues in good health
32	H. B.	60	M	March 1940	Extensive roentgen ray therapy with diminishing response	November 1944	4	20	6	Fever, abdominal pain disappeared; peripheral lymphadenopathy and abdominal mass decreased in size; therapy with the drug supplemented in December 1945 by local roentgen ray to abdominal mass (1,500 r)

TABLE 4.—*Résumé of Cases of Lymphatic Leukemia Treated with Methyl-Bis (Beta-Chloroethyl) Amine Hydrochloride*

Case	Patient	Age	Sex	Onset of Disease	Previous Therapy and Results	Courses of Treatment: Date of First	Courses of Treatment: No. Given	Period of Observation in Mo.	Average Duration of Remissions in Mo.	Comment
33	G. M.	59	M	1940	Extensive roentgen ray with initial response only	March 1943	3	6	3	Partial relief of symptoms during 6 mo. of observation; died after 3d course without appreciable response
34	M. G.	61	M	1939	Roentgen ray with remissions averaging about 3 mo.	September 1943	3	18	2 to 3	Abdominal masses and lymphadenopathy decreased in size; patient able to return to work; died August 1945 after operation to relieve bowel obstruction
35	R. H.	64	F	1943	Previous therapy with roentgen ray gave responses of about 1 mo.	September 1943	2	15	2 to 4	Abdominal masses, lymphadenopathy and peripheral edema decreased; died from extension of disease in January 1946; roentgen ray therapy attempted again had not been effective
36	F. T.	63	M	1942	No previous therapy	April 1944	1	11	5+	Severe uremia present before treatment; uremia slowly progressed but general result of treatment with the drug was good; died 3/27/45 of uremia
37	C. P.	42	M	Nov. 1943	None	November 1944	2	20	6 to 12	Fever, lymphadenopathy and splenomegaly disappeared; continues to feel well and is working
38	E. S.	63	M	1938	None	December 1944	1	14	2 to 3	Only 1 treatment with the drug given; roentgen ray therapy then initiated with end of the drug-induced remission; response to roentgen ray was negligible; patient died 4/30/45
39	V. N.	53	M	1943	None	October 1944	1	21	21	Only 1 treatment given; remission hematologically and symptomatically continues
40	M. K.	64	M	Jan. 1945	None	Oct. 10, 1945	1	10	0	Brief hematologic response but no symptomatic response; is now under treatment with radioactive phosphorus

COMMENT

In approaching a decision on the efficacy of this drug it is useful to compare it to other leukotoxic materials which have been used in treating blood dyscrasias. Roentgen rays and benzene are outstanding examples; each of these may produce a comparable change in the

hemopoietic system by reducing it to a reticular stroma with scattered reticulum cells from which regeneration must occur. The sequence described by Woronow [5] and Wallbach [6] subsequent to the administration of benzene are in all respects similar to those we have described as occurring after the injection of methyl-*bis* (β-chloroethyl) amine. Roentgen rays may likewise produce a pathologic picture in hemopoietic tissue which is indistinguishable from that produced by the drug. In common these materials attack the mature and immature cells of the hemopoietic system. There appears to be some difference in the degree of damage to certain cell types and in the ability of the cell to regenerate from the injury. Benzene appears to attack the marrow to a greater extent than either roentgen rays or the nitrogen mustard, both of which, although injuring the bone marrow, appear to produce a greater damage to the lymphatic tissue. Regeneration of the hemopoietic system from injury by benzene is frequently incomplete, and its use as a therapeutic agent has been largely discontinued because of the difficulty in disease; lymphosarcoma; sympathoblastoma; multiple myeloma; myelogenous leukemia, acute and chronic forms; polycythemia rubra, and lymphatic leukemia, acute and chronic forms.

The dosage of the drug was 0.1 mg. per kilogram of body weight given in courses of one to seven daily injections.

The usual immediate toxic reaction of nausea and vomiting manifests itself within three to four hours after administration. A delayed but more serious toxic manifestation is the lymphopenia, neutropenia and thrombocytopenia which almost invariably occurs within the first three weeks. The rapidity and severity with which these latter reactions become manifest depends on the sensitivity of the patient to the drug, on the disease concerned and on the total amount of the drug given in a course. With courses of four or more injections leukopenias of 2,000 cells per cubic millimeter are common. Anemia may develop but is usually minor. The hematologic changes observed in the peripheral blood are paralleled in the bone marrow. Serial sternal puncture material and rib biopsies on selected patients indicate that an extreme degree of destruction may occur. Recovery of the bone marrow, however, as indicated by aspiration and biopsy studies, is complete after varying intervals. The constituents of the peripheral blood otherwise return to normal values.

TABLE 5.—*Résumé of Cases of Polycythemia Rubra Treated with Methyl-Bis (Beta-Chloroethyl) Amine Hydrochloride*

Case	Patient	Age	Sex	Onset of Disease	Previous Therapy and Results	Courses of Treatment: Date of First	Courses of Treatment: No. Given	Period of Observation in Mo.	Average Duration of Remissions in Mo.	Comment
41	S. L.	47	M	Before 1944	Phlebotomies	January 1945	2	17	6 and 12+	Symptoms of dizziness, sluggishness and headaches disappeared within 3 wks. of initial treatment with the drug; blood has remained within normal limits over 18 mo. period
42	L. W.	60	M	1940	Phlebotomies; radioactive phosphorus without hematologic remissions	January 1945	2	17	8+	Symptomatic relief since treatment initiated in January 1945; erythrocyte count however, which was about 10×10^6 per cu. mm. has gone down very slowly
43	A. O.	47	M	1936	Phenylhydrazine; phlebotomies; radioactive phosphorus with remissions of 6 mo. with the latter	January 1945	1	6	6+	Immediate relief of symptoms and blood normal within 1 mo. after treatment; continues in normal range
44	F. L.	55	F	Prior to 1938	Phenylhydrazine; phlebotomies	April 28, 1946	1	3	3+	Symptomatic and hematologic remission continues
45	W. B.	45	M	1942	Phlebotomies; radioactive phosphorus with remission of 1 yr.	March 20, 1946	1	4	4+	Complete symptomatic and hematologic remission continues

controlling the dosage, the variations in individual susceptibility and the occurrence of fatal cases of aplastic anemia.

We have attempted to detect an inherent aplastic reaction produced by the cumulative effect of repeated treatment with methyl-*bis* (β-chloroethyl) amine hydrochloride, but have seen no evidence to indicate such a course of events. In the 54 cases reported here (this figure excludes the 5 cases still under observation) we have not seen the severe purpura or anemia so common after exposure to benzene, and hematologic recovery has been invariable.

SUMMARY AND CONCLUSIONS

Since March 1943, a series of 59 patients with neoplastic and allied disease of the hemopoietic system have been treated with methyl-*bis* (β-chloroethyl) amine hydrochloride. The diagnosis of each patient was confirmed by biopsy or sternal puncture. The diseases treated with this drug include: Hodgkin's disease; lymphosarcoma; sympathoblastoma; multiple myeloma; myelogenous leukemia, acute and chronic forms; polycythemia rubra, and lymphatic leukemia, acute and chronic forms.

Patients have been observed after single or repeated courses of methyl-*bis* (β-chloroethyl) amine hydrochloride from two to thirty-three months. The clinical remissions vary from zero to eighteen months. Certain disease processes such as acute leukemia and multiple myeloma failed to respond to treatment. The clinical results in most cases of myelogenous leukemia and in a few cases of lymphatic leukemia, lymphosarcoma and Hodgkin's disease were not satisfactory. Encouraging results have largely been confined to Hodgkin's disease. The common symptoms of fever and malaise are frequently relieved within a short period after the initiation of treatment. Lymphadenopathy, splenomegaly and hepatomegaly usually regress rapidly. Repeated courses of treatment with the drug have produced further remissions. In certain cases of Hodgkin's disease classified as roentgen ray resistant significant clinical remissions have been produced.

5. Woronow, A.: Ueber die morphologischen Veränderungen des Blutes und der bluterzeugenden Organe unter dem Einflusse des Benzols und dessen Abkömmlinge, Virchows Arch. f. path. Anat. **271**:173, 1929.
6. Wallbach, G.: Untersuchungen über die unterschiedliche Wirkung einiger leukocytenvermindernder Substanzen, Ztschr. f. d. ges. exper. Med. **68**: 621, 1929.

PENICILLIN SPRAY BY BULB ATOMIZER IN RESPIRATORY INFECTIONS

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Penicillin spray, as used in this report, is produced by a hand-operated bulb atomizer and is utilized by inhalation. The patient holds his breath at the end of the inspiration, allowing the suspended penicillin to settle on the infected mucous membranes. The terms aerosol penicillin and penicillin spray are used synonymously. An aerosol is a fine suspension of a liquid or solid in a gaseous medium.

Penicillin is perhaps the greatest life-saving drug today. The greatest drawback to its general use by the country practitioner especially, and to a lesser degree by his urban brother, in this day of overcrowded hospitals and scarcity of nurses is that its use by the accepted intramuscular or intravenous routes requires either hospitalization or the employment of two trained nurses. The use of a hand atomizer to produce a spray of penicillin, which is inhaled to medicate infections of the respiratory tract, removes the aforementioned limitations and makes the drug available in the remotest areas. Penicillin spray, or aerosol penicillin, has been used in a large number of cases of respiratory infections with excellent results. Vermilye [1] reported a series of over 200 cases in which aerosol penicillin was effective. "Over 200 patients with various upper respiratory conditions, or manifesting allergic reactions to an upper respiratory infection, have been treated with aerosol penicillin" he states. "It must be borne in mind that such bizarre complaints as migraine, eczema, rosacea, duodenal pain, allergic colitis, extreme fatigue and even mild psychoneurotic symptoms may in fact be either due to, or aggravated by, allergy to the presence of a mild chronic or acute upper respiratory infection." He also reports good results in some cases of asthma. Segal and Ryder [2] reported good results in 21 cases of serious respiratory infection-pneumonia, lung abscess and bronchiectasis.

This article is written by a general practitioner especially for other general practitioners. In its nature it is more a preliminary report than a scientific article, since penicillin spray has been used for only a short time and there are too few cases reported to be of statistical significance. However, this series shows that the use of penicillin in this way is of definite value and certainly justifies further clinical trials.

The employment of a spray of penicillin which is inhaled offers a logical, efficient method of combating infections of the respiratory tract, nasopharynx and accessory nasal sinuses. Its use resembles a well planned military maneuver, a strong attack from the rear while resistance is maintained on the flanks and frontally. Respiratory infection in the vast majority of cases enters the body by the nasopharynx. The various natural body defenses contain the attack by maintaining pressure frontally and on the flanks; when this is supplemented by a strong rear attack of penicillin spray by inhalation the infection is overcome. The penicillin not only has a strong local effect but is absorbed into the blood stream and aids the natural body defenses as well, by supplementing their frontal attack. Penicillin not only has an anti-infective effect, as is well known, but it also has a definite local soothing effect which relieves such discomfort as soreness in the throat, painful, frequent coughing and the sensation of dryness in the mucous membranes. Penicillin spray can be used by any one except the very young; it has been used successfully in children down to the age of 17 months. It could be used by mask in the unconscious and in infants, although I have had no experience with this method.

As far as can be ascertained, this is the first series of cases reported on the use of penicillin spray produced by a hand-operated or bulb atomizer. Previous series have used a power-operated atomizer, the power being supplied by an oxygen tank whose pressure transformed penicillin solution in a nebulizer into a spray. A power atomizer is certainly more scientific, but the ordinary bulb atomizer is more practical, especially from the point of view of portability and also because of its economy and availability. Undoubtedly the oxygen under pressure supplies an added therapeutic aid to an extremely toxic patient which may tip the scales in his favor, but when this aid is necessary the patient should be hospitalized. If the patient is too sick to operate the atomizer, an infrequent occurrence if treatment is started early, this can be done by any attendant.

The following series is reported to make this method available to the medical profession. It is realized that there are no radiologic or laboratory data because the patients were all treated in the home, with 2 exceptions. Also this series was worked up at the height of an epidemic of influenza.

RATIONALE

The absorptive properties of the lung are not properly appreciated. It is hard to realize that the inner surface of the lung has an area five hundred times as great as the body surface and, as Segal and Ryder [2] have reported, drugs given as aerosols are absorbed so rapidly that their effect is similar to that of an intravenous injection. Furthermore, Krueger and others [3] demonstrated in the lungs of monkeys and mice, using india ink and radioactive chromic phosphate as indicators, that, with inhalation, material was uniformly distributed and penetrated to the outermost air sacs of the lungs at the end of the bronchial tree. It is thus possible by inhalation to obtain a high local concentration where it is most needed as well as varying levels of the blood. Since penicillin with a concentration of 250,000 units per cubic centimeter has been aerosolized and inhaled there appears to be little doubt that large amounts of penicillin can be introduced by this method. When it is realized that 18 cc. can easily be used in a day, it is thus theoretically possible to give 45,000,000 units daily. Penicillin seems to act in a more efficient manner when given by spray than by injection. It is common to give 160,000 units daily by the intramuscular route in pneumonia, whereas in treatment of 1 case of pneumonia in this series 40,000 units was given daily for four days, a total dosage of 160,000 units in all. In other words, the total dose in this case treated by spray would supply only one day's dose if given intra-

1. Vermilye, H. N.: Aerosol Penicillin, J. A. M. A. **129**: 250 (Sept. 22) 1945.
2. Segal, M. S., and Ryder, C. M.: Penicillin Aerosolization in the Treatment of Serious Respiratory Infections: Preliminary Report, New England J. Med. **233**: 747, 1945.
3. Krueger, A. P., and others: The Inhalatory Route for Prophylaxis and Treatment of Experimental Influenza: The Distribution of Inhaled Material; Immune Serum in Prophylaxis and Treatment, Am. J. M. Sc. **207**: 40, 1944.

V 13
1946

muscularly. This saving of penicillin is apparently due to the fact, that, first, the greatest concentration of penicillin is directly on the infected site, the air sacs, and secondly, it is absorbed into the blood stream and thus has a systemic effect as well. This fact has been proved several times in other series of cases.

The rationale of the use of penicillin spray in respiratory infections is to get penicillin in contact with the infective process, just as is done by its injection into body cavities in empyema and septic joints. Probably it is more efficient, since penicillin is more uniformly dispersed in the form of a spray than when its dispersal depends on its solution in an exudate. Since the function of the accessory nasal sinuses is to warm and moisten inspired air, the distribution of penicillin should also be efficient in these regions. When the sinus openings are blocked, the spray may be more efficiently used when supplemented either by the use of a vasoconstrictor in the spray or by nose drops. However, vasoconstrictors are probably unnecessary since the usual cause of blockage is an infective process which is overcome by the penicillin. As is well known, the most frequent invaders and inhabitants of the respiratory tract are pneumococci, streptococci and staphylococci, which are all efficiently combated by penicillin. In virus pneumonia it should be borne in mind that it is not the penicillin resistant virus which kills but the penicillin sensitive secondary invaders such as pneumococci.

EXPERIMENTAL AND OTHER EVIDENCE ON AEROSOL PENICILLIN

Bryson, Sonsome and Laskin [4] report that the chemical and bacteriostatic properties of penicillin are not altered when it is transformed into an aerosol. Ground lungs from mice exposed to aerosol penicillin show a bacteriostatic activity not present in controls. It is stated that effective penetration of the respiratory bronchioles and alveoli is best attained by small particles; therefore the finer the spray, the more efficient the effect.

Levels of Penicillin in the Blood.—Recovery of penicillin in the urine may be accepted as proof that it has been present in the blood. Bryson and his co-workers [4] reported that 60 per cent of aerosolized penicillin has been recovered in the urine within twelve hours, comparing favorably with an average recovery of 60 per cent after intravenous injection. In consideration of this fact, one must remember that aerosol penicillin has an important local bacteriostatic effect before absorption by the blood stream as well as its usual effect after absorption. Segal and Ryder,[2] using 20,000 units every two hours (aerosol), obtained effective levels of penicillin in the blood ranging upward from 0.028 units per cubic centimeter. They also stated: "Generally speaking, higher blood levels were obtained in those with extensive lung involvement of a pyogenic type—that is, those with pneumonia or lung abscess." A single striking exception in their series was a patient with type I pneumonia involving two lobes in whom it was impossible to obtain a penicillin level in the blood, but whose clinical response was nevertheless striking. Therefore, it is not necessary to produce levels of the drug in the blood to obtain a rapid recovery, which is all that matters to the patient.

4. Bryson, V.; Sonsome, E., and Laskin, S.: Aerosolization of Penicillin Solutions, Science **100**: 33, 1944.

Advantages of Aerosol Penicillin.—The advantages of aerosol penicillin are manifold, and a summary of them includes these points:

1. The absence of toxicity in contrast to that of the sulfonamides. This is an important consideration to the general practitioner who sometimes finds it difficult to observe closely his patients.

2. The absence of dangers due to untrained personnel using the intramuscular route of administration.

3. The ease of transporting and caring for the materials, the atomizer and penicillin. In winter when respiratory infections are most prevalent, it is also easiest to take the proper care of penicillin.

4. The availability of materials. Atomizers can be easily obtained and are cheap. I have six atomizers in continuous use. When 1 patient is through with an atomizer it is easily cleansed with soap and water for the next. Persons suffering from recurrent or chronic respiratory infections are advised to buy their own atomizers.

Boiled and cooled water was used exclusively as the solvent for penicillin in this series of cases.

5. Painless administration. This is an important factor in nervous or young patients. The screams of 1 child treated intramuscularly still ring in my ears, in contrast to which, most children take the use of aerosol penicillin as a game.

6. The saving in penicillin. In this series of cases, small amounts of penicillin were used for two important reasons; first, because penicillin was scarce and second, because small doses were sufficient. One case of typical moderate pneumonia was treated with a total of only 160,000 units of penicillin in four days, in contrast to the usual intramuscular dose of 160,000 units a day.

7. Prophylactic use. One hesitates to use a valuable drug which is relatively scarce as well as relatively expensive in large doses unless confronted with a seriously ill patient. Also, one hesitates to make a pin cushion of a patient unless it becomes necessary. With the efficient painless use of penicillin as a spray these objections are removed, and one is more inclined to use this drug against respiratory infections in their early stages.

8. The treatment of "key" persons. Often, a general practitioner views with dread the development of an illness in the mother of a home where there already is sickness. She is the keystone of the family arch, and it is a serious thing for every one when she becomes sick. Treat her early with penicillin spray, and she will be able to carry on. This holds true for "less important" people as well, for wage earners, business executives and even physicians.

9. Local comfort (rather than discomfort). The use of penicillin spray has a remarkably soothing local effect in addition to its therapeutic effectiveness. Dry, irritated mucous membranes are moistened, relieving the soreness of the throat as well as the tracheal discomfort and burning. The effect on a tight, frequently recurring cough is dramatic; it rapidly becomes much less frequent and less painful and expectoration is made easy.

10. The pleasant taste of penicillin. The taste of penicillin resembles that of a dilute acetone solution.

11. The small cost. The economy of aerosol penicillin is an important consideration.

12. The absorption of inhaled penicillin. The fact that inhaled penicillin spray is absorbed and can attain an effective level in the blood suggests that perhaps sites of infection other than those in the respiratory tract may be treated in this manner.

13. Compound fractures of the skull. In such fractures, it is suggested that the nasopharynx and the auditory canal could be rid of most pathogenic organisms by the use of penicillin spray, thus lessening the chances for the development of meningitis.

USE OF AEROSOL PENICILLIN DURING AN EPIDEMIC OF INFLUENZA

In this series of cases, the epidemic of influenza which infected most of these patients began in this locality about Jan. 3, 1946 and has now tapered off. The influenza was a respiratory infection which usually began with a slight sore throat and spread upward into the nasal sinuses and/or downward into the lungs where a tracheobronchitis developed. In some of the patients, especially those who tried to "work it off," there developed moderate or severe pneumonias. The use of sulfadiazine (and, less often, sulfathiazole) helped these nonpneumonic patients a good deal, apparently by reducing the secondary infection. The influenza when uncomplicated by a sinusitis, bronchitis or pneumonia appeared to be a mild disease with a temperature of 99 to 100 F. accompanied with generalized aching for a day or so. The rationale of giving penicillin in treatment of moderate cases of influenza was to control the secondary infection and thus to prevent complications.

Technic.—1. Equipment Needed: One rubber-capped bottle of sodium penicillin (100,000 units; one 10 cc. syringe and needle; a few ounces of sterile, cold, tap water, and two sterile 2 drachm (7.5 cc.) vials and corks. Place these instruments in a pan containing one inch of tap water; cover, boil three minutes and cool. Do not pour off the water; use it for making the solution.

2. Preparation: A. Stock solution of penicillin. Using a syringe, add 10 cc. of cold, sterile tap water to the 100,000 unit bottle of penicillin powder, and allow it to dissolve; this gives a concentration of 10,000 units per cubic centimeter. Darker brands of penicillin powder are not as good for inhalation as lighter ones—they seem to be a little more irritating, though this is not really an important point.

B. Dilutions of the stock solution of penicillin for the atomizer.

(1) 100,000 units in 4 drachms (15 cc.). Withdraw 10 cc. of the stock solution and place 5 cc. in each of the two sterile 2 drachm (7.5 cc.) vials, then add sterile water up to the neck of the vial and cork. Do not add too much water or you will have difficulty in keeping the vial corked. It is well to fasten the cork with small pieces of adhesive down the sides of the vial, especially if the solution is to be mailed.

(2) 80,000 units in 4 drachms (15 cc.). Withdraw 8 cc. of the stock solution and place 4 cc. in each of the two sterile 2 drachm (7.5 cc.) vials; proceed as in (1).

(3) 60,000 units in 4 drachms (15 cc.). Withdraw 6 cc. of the stock solution and place 3 cc. in each of the two sterile 2 drachm (7.5 cc.) vials; proceed as in (1).

(4) 40,000 units in 4 drachms (15 cc.). Withdraw 4 cc. of the stock solution and place 2 cc. in each of the two sterile 2 drachm (7.5 cc.) vials; proceed as in (1).

3. Administration: The patient is instructed as follows: empty the lungs thoroughly by exhaling strongly and slowly. Place the atomizer tip in the mouth just inside the teeth and on beginning inhalation press the atomizer bulb; continue rhythmic spraying throughout inhalation, then stop. Hold the breath at full inspiration as long as possible, then exhale slowly and gently through the nose. Continue this for ten minutes at first, then for ten minutes in an hour and then for ten minutes once every four hours when awake. It is important to exhale strongly to empty the lungs before beginning to spray, but after the first inhalation do not expire too thoroughly because some penicillin spray may be blown out of the lungs. It is important to hold the breath as long as possible at the end of the spray inhalation, in order to allow the penicillin to be deposited in the lungs and respiratory tract. Inhalation should be slow and not too deep, otherwise coughing may be started. (If the patient is dyspneic or there is some irritation on spraying, a few inhalations can be made without using the spray, then recommence the spray.) It is a mistake to use the atomizer too vigorously because this gives a spray with large droplets which is not only inefficient but liable to condense in the nose or on the soft palate instead of going into the lungs. If penicillin condenses in the nose or throat, the natural impulse is to spit it out or to swallow it; do not do so, or the penicillin is wasted. Wait a minute until the irritation disappears. If there is an accompanying sinusitis, spray as instructed, but alternate nostrils. The length of inhalation varies with each patient and has to be worked out individually. It is important to get the twenty-four hour dose in twenty-four hours.

As a help to the patient I place four strips of adhesive on the sides of the atomizer to indicate a division into quarters, so that the amount of solution to be taken can be gaged fairly accurately. In sinusitis uncomplicated by laryngitis or tracheobronchitis the dosage of penicillin solution should be 2 drachms (7.5 cc.) instead of the usual 4 drachms (15 cc.).

4. Atomizers: A. DeVilbiss No. 15. This gives a fine spray but is not quite as portable as the one described in *B*. However, it is well made and is suitable for this method.

B. Atlas No. 82 (DeVilbiss made). This atomizer gives a slightly coarser spray and is cheaper than the preceding one. It is compact and portable and is perhaps the best for general use. This atomizer was the one most commonly used in this series.

C. Glaseptic atomizer. This type of atomizer gives the finest spray and therefore is particularly efficient. It has two main drawbacks; first, it is easily broken because it is constructed of drawn glass and second, it is tedious to use because of the time needed to get the entire dose.

5. Precautions: Penicillin must be kept cold or it loses its power. Freezing does not hurt it but may break the container. A penicillin solution apparently keeps its strength about a week at refrigerator temperature. There is no danger of overdosage by any method of administration. Sulfa resistant bacteria are not penicillin resistant and vice versa.

6. Dosage: The question of dosage is not entirely settled at present, and of course no dosage is absolute but varies with the virulence of the infection and the condition of the patient. It has been my experience that an amazingly small amount of penicillin has been effective; but it must be remembered that this series of cases is small, and it may be that the organisms were more susceptible than the average to penicillin. It is

V 13
1946

possible to give at least 45,000,000 units a day by this method, a dosage which, of course, would never be indicated, and it is equally possible to give a minute dosage. With regard to the amount of solution given in twenty-four hours, I have always used 4 drachms (15 cc.) but I believe that at least double this amount could easily be used. Segal and Ryder [2] have advised, in treatment against pneumonia, 25,000 units given every two hours for six doses or more, then every three hours for sixteen doses or more, both depending on the clinical response of the patient. They have also reported excellent results obtained on this dosage in patients with bronchiectasis and abscess of the lung.

Vermilye [1] is somewhat obscure as to his dosage, but he gave 1 patient with type XX pneumonia 40,000 units four times a day for a week, then twice a day for two weeks.

In my experience the following doses, though small, have been effective and their use will be continued when indicated until it is apparent that they are not adequate.

The amounts of penicillin shown in the accompanying table are twenty-four hour dosages to be divided into four doses by the patient and to be used at four hour intervals when awake. The twenty-four hour dosage is placed in the atomizer and the amount is easily gaged by means of four adhesive strips on the outside of the bottle. All these doses are dispensed in 4 drachms (15 cc.) of water except in uncomplicated sinusitis when 2 drachms (7.5 cc.) are used.

REPORT OF CASES

Pneumonia.—There were 5 cases diagnosed as pneumonia in this series.

CASE 1.—*History.*—C. B., a single white man aged 27, a butcher, was seen Jan. 13, 1946. He had a cough, a pain in the left side, chills and rusty sputum for twelve hours. The past history was irrelevant. The temperature was 101 F., and the pulse rate was 110.

Physical Examination.—Examination disclosed a well nourished adult man, with his eyes bright, his appearance toxic and with a frequent painful cough. For a handbreadth at the base of the left lung there were dulness and distant breath sounds, and fine moist rales were heard in this area.

Treatment.—Penicillin was administered in dosages of 50,000 units January 13, 40,000 units January 14, 40,000 units January 15, 35,000 units January 16 and 25,000 units January 17 and 18.

Course.—The cough became loose, infrequent and painless in twelve hours. The temperature fell to 99 F. in twelve hours, rising to 99.4 F. at night; thereafter it was normal, except for the second night when it was 99 F. The general response was striking. Because he felt so much better after sixteen hours of treatment the patient got out of bed but felt weak. He got up on the third day and had no relapse.

CASE 2.—*History.*—R. S., a white schoolboy aged 8, was seen Feb. 8, 1946. His throat was raw, and he had a frequent painful cough with generalized aching for the past ten hours. He had always been pale and poorly fed. The temperature was 100 F. and the pulse rate was 100.

Physical Examination.—The boy was listless and appeared toxic. For a handbreadth at the base of the left lung there was an impaired note with diminished breath sounds and vocal resonance.

Treatment and Course.—He was put on a sulfathiazole regimen for twenty-four hours, when he became worse; he appeared dull, his cough was worse and he was nauseated. On February 9, the temperature was 103 F., the pulse rate was 120, and there were three patches of bronchial breathing and moist rales, two at the base of the left lung, the third in the right axillary region. Penicillin spray, 40,000 units a day for four days, was given. On February 11 the temperature was normal, the pulse rate 80, the cough infrequent, and it was hard to keep the patient in bed. There was no relapse. The diagnosis had been bronchopneumonia.

CASE 3.—*History.*—D. McL., a single white man aged 25, a college student who had always been healthy and robust, contracted influenza at college. He had a general malaise, nausea and diarrhea, with a slight, painful cough and a temperature of 104 F. for forty-eight hours. Then his temperature dropped to normal and he drove 45 miles to his home where generalized aching, headache and sore throat, a more severe cough and a temperature of 101 F. developed. He went to bed and treated himself with acetylsalicylic acid compound and fluids. For seven days the patient continued to get worse until Jan. 25, 1946 when he was first seen by a physician.

Examination.—He was toxic looking, his cheeks were flushed and his eyes were bright; he had a frequent, painful cough and expectorated thick mucopurulent material. The temperature was 103 F. and the pulse rate was 116. Examination of the lungs revealed dulness with bronchial breathing and moist rales for a handbreadth at the base of the right lung.

Treatment.—Penicillin was administered as a spray in dosages of 25,000 units in twelve hours on January 25, 80,000 units in twenty-four hours on January 26 and 40,000 units in twenty-four hours on each of the next three days, January 27, 28 and 29.

Recommended Dosage of Aerosol Penicillin

1. Pneumonia		
Severe	24 hour dosage	100,000 units, spray every 4 hours
Moderate	24 hour dosage	60,000 units, spray every 4 hours
Mild	24 hour dosage	40,000 units, spray every 4 hours
2. Bronchitis		
Severe	24 hour dosage	60,000 units, spray every 4 hours
Moderate	24 hour dosage	40,000 units, spray every 4 hours
3. Sinusitis		
Severe	24 hour dosage	60,000 units, spray every 4 hours
Moderate	24 hour dosage	40,000 units, spray every 4 hours
4. Laryngitis		
Severe	24 hour dosage	60,000 units, spray every 4 hours
Moderate	24 hour dosage	40,000 units, spray every 4 hours
5. Sore throat as for laryngitis.		
6. Disease of the middle ear. It is suggested that in disease of the middle ear 40,000 units in 2 dr. (7.5 cc.) of water would be a great aid in clearing up the infection of the throat		

Course.—The response in this case was spectacular. The temperature of the patient fell to 100 F. in twenty-four hours and remained normal after forty-eight hours. His cough which had been so troublesome was almost absent in eighteen hours. The toxic appearance vanished in twelve hours. His appetite returned in eighteen hours; for six days prior to this he had been subsisting entirely on grapefruit juice and water because he had no desire to eat. On January 30 he walked a quarter of a mile against orders and with no apparent ill effect. He returned to college Feb. 6, 1946 and since then has had no trouble.

CASE 4.—*History.*—A. B., a married white man aged 40, had always been a hard working, husky farmer and a good athlete. On Jan. 12, 1946, there developed malaise, a painful tight cough, generalized aching and a headache; the temperature was 100 F. He worked for twenty-four hours with these symptoms, but on January 13 he had to go to bed, and he took a patent cough medicine. When he was seen January 15 he looked toxic and had a frequent painful cough.

Examination.—The temperature was 103 F., the pulse rate was 100. An impaired note was heard at the base of the left lung with bronchial breath sounds and a few moist rales.

Treatment.—Penicillin was administered as a spray on January 15, 35,000 units in twelve hours, on January 16, 80,000 units in twenty-four hours and on January 17, 50,000 units in twenty-four hours. Treatment with penicillin was then discontinued because no more could be obtained. A total of 165,000 units of penicillin spray had been given in seventy-two hours.

Course.—The cough became less frequent, painless and loose in twelve hours. The patient stayed in bed January 18 but got up on January 19. He was weak for four or five days

132
946

but had no relapse. His wife had the same symptoms without pneumonia and took sulfadiazine to no effect. She ran a fever of 100 to 101 F. for five days and stayed in bed for seven days, then she got up before she was fully recovered.

CASE 5.—*History.*—F. B., a white man aged 76, was a farmer who weighed 150 pounds (68 Kg.) when first seen on Feb. 22, 1946. He had been a hard worker and rarely missed a day's work. His illness began February 21 with generalized aching accompanied by a painful dry cough which came every fifteen minutes in spasms of about six rapid coughs. He could not work on February 22, when the symptoms of the previous day were more pronounced and accompanied by chilliness, pain in the left anterior portion of the chest on coughing and a temperature of 100 F. At 11 p. m. he began to have chills which shook the bed, and these continued all night in spite of the use of six blankets.

Examination.—On February 23 all symptoms were increased together with decided weakness and moderate stupor. The patient was moderately disoriented and took no interest in his surroundings. The temperature was 101 F., the pulse rate was 80 and the blood pressure 130 systolic and 90 diastolic. (In July 1944 the blood pressure had been 180/100.) There was an impaired percussion note for a handbreadth at the bases of both lungs, with diminished breath sounds and a few moist rales.

Treatment and Course.—He was given sulfadiazine, 1.5 Gm. followed by 1 Gm. an hour later, then 0.5 Gm. every three hours. On February 24 the temperature was 103 F. Weakness, stupor and other symptoms were the same as on February 23. The patient refused to take fluids and wanted to be left alone. In view of his poor response to sulfadiazine therapy and his refusal to be hospitalized, he was given penicillin spray with a dosage of 80,000 units every twenty-four hours starting at 11 a. m. At 4 p. m. his temperature was still 103 F. but he was coughing less, and in the evening he began to talk rationally. On February 24 he showed definite improvement with very little cough. The temperature was normal during the day, rising to 99 F. at night. The pulse rate was 70. The patient carried on a normal conversation and joked; he took fluids well and that night requested food for the first time. On February 25 the pulse rate was 54, the temperature 99 F. and 80,000 units of penicillin were administered. The cough was infrequent and loose, and the patient wanted to talk and tell stories. He was sitting up in bed reading a farm implement catalog. An examination of the lungs verified the observations made before and in addition disclosed an area 2 inches wide in the left axillary region with bronchial breath sounds, an impaired note and moist rales. He was given penicillin, 60,000 units in twenty-four hours. On February 26 his improvement continued; the penicillin dosage was 60,000 units in twenty-four hours.

Comment.—This patient was the most seriously ill of all those treated with penicillin spray. A disoriented 76 year old man with bronchopneumonia who was not improving on sulfadiazine therapy, he responded rapidly to treatment with penicillin spray.

Bronchiectasis with Pneumonia.—Two cases in this series were diagnosed as bronchiectasis with pneumonia. In both there was a long history of acute and of chronic respiratory infection, with examinations of the chest repeatedly positive. There had been no injection of iodized poppy-seed oil 40 per cent, but the presumptive diagnosis was a mild degree of bronchiectasis with little toxemia.

CASE 6.—*History.*—Mrs. M. R. was an obese, white housewife, aged 52. In 1939 she had severe pneumonia with delirium for three days and was confined to bed for one month. This slowly reacted to treatment with sulfapyridine, but the chest infection persisted after the acute attack had subsided. Since 1939 she had had a chronic cough with the expectoration of mucopurulent sputum which had no smell. In May 1945 she had a "cold on her chest" for which she took cough medicine, and three weeks later she presented herself for examination. At that time she had dulness, bronchial breathing and coarse, moist rales for a handbreadth at the base of the left lung. The temperature was 99 F. and the pulse rate was 96. The sputum was mucopurulent and moderate in quantity but not foul. After she was given sulfadiazine for three weeks, the symptoms and temperature gradually subsided but the cough, chest observations and sputum persisted to a mild degree. Repeated examination of the sputum was negative for Mycobacterium tuberculosis. A roentgenogram showed increased bronchial markings throughout the lung fields, especially well defined at the base of the left lung.

Examination.—On Jan. 7, 1946 another cold on her chest developed. The temperature was 102.5 F., and the pulse rate was 110 with slightly blood-tinged, mucopurulent sputum. There were dulness, bronchial breath sounds and a moderate number of moist rales at the base of the left lung.

Treatment and Course.—She was given 100,000 units of penicillin by spray daily for two days, and the temperature fell from 102.5 to 100 F. in this period. Thereafter it remained normal except for a daily excursion to 99 F. until January 16. She had a total of 530,000 units from January 11 to 23, or an average of 44,160 units a day. The patient felt weak although the cough and the expectoration of sputum were much abated. A gradual improvement took place subjectively, but due to the persistence of a few rales and an impaired note at the base of the left lung penicillin therapy was renewed on February 5 with a dosage of 60,000 units a day until February 13. This resulted in a gradual decrease in her weakness and an improvement in appetite. On February 24 her chest was clear except for an impaired note at the base of the left lung, and she felt well.

CASE 7.—*History.*—J. B., a white schoolgirl aged 10, weighed 67 pounds (30 Kg.). This girl had pneumonia eight times in the last ten years. Her chest was never clear and she had a chronic cough with expectoration. Tuberculin tests have been negative; the sputum had been negative for Mycobacterium tuberculosis. A roentgenogram showed increased bronchial markings at the base of the right lung in July 1945. She had taken the various sulfonamide compounds so many times that she was sensitive to all of them. From Dec. 1, 1945 to Jan. 3, 1946 she had a daily afternoon temperature of 99 to 100 F. On Jan. 5, 1946 she contracted a cold and her temperature rose to 101 F. with a pulse rate of 100.

Examination.—Examination revealed a toxic, listless girl, well nourished but somewhat pale and flabby looking. There was a perceptible dull note at the base of the right lung for a handbreadth, with bronchial breath sounds and moist rales in this area.

Treatment.—This was the first patient on whom I used penicillin spray, and some of my troubles are here noted. It was impossible to hospitalize the girl. Sulfadiazine was given for twenty-four hours but was discontinued because a rash appeared and there was no clinical improvement. Then the administration of penicillin as a spray was begun; 3,000 units per twenty-four hours were given for three days, 5,000 units per twenty-four hours for two days, 3,000 units per twenty-four hours for four days and 15,000 units per twenty-four hours for four days.

Course.—In spite of the minute dosage of penicillin given to this girl, her temperature fell from 101 F. to normal in twenty-four hours. Her cough became loose and she felt better generally. On the second day the penicillin was useless, due to the inadvertent use of warm water as a solvent; in twelve hours she again felt weak, her cough returned with sputum, and her temperature rose to 101 F. This was immediately reduced by active penicillin. On January 19 the use of penicillin was discontinued for fear that a penicillin-resistant strain of organisms would develop and because she was so much better. In the patient's words, "I feel just like I do in summer when I have no cold." There were still signs of disease in her chest; an impaired note and a few moist rales, the fewest heard for eight months. On February 5, penicillin therapy was recommenced on a dosage of 40,000 units each twenty-four hours with the hope of clearing her lungs. It was continued until February 12. The signs in her chest diminished but did not clear up entirely; the percussion note was still impaired, but rales were fewer and the temperature, which was taken

V 13
1946

three times a day, had been normal since February 8. It should be emphasized that prior to penicillin therapy, she had run a daily temperature for over a month. On February 19 penicillin therapy was begun again in the same dosage for seven days. On February 21, while her three brothers and her mother had influenza, her temperature went up to 100 F. in the evening, but since then it has been normal at all times. She did the housework for four days while the others were in bed with influenza. This case illustrates the fact that the "flu" organism is not susceptible to penicillin and that influenza is, in itself, a mild disease whose complications are caused by invaders sensitive to penicillin. She is carrying on with weekly courses of penicillin in the hope of clearing up the disease in her chest permanently.

Segal and Ryder[1] have reported better results obtained with penicillin given by inhalation than with the drug used intramuscularly in the preoperative treatment of bronchiectasis. They also report 3 cases of bronchiectasis cured by this method.

Laryngitis.—Laryngitis has always been a veritable bête noire, or worse, to physicians and patients alike. The following 3 cases show that penicillin spray had a striking, immediate effect, in contrast to the usual slow recovery of a patient from this disease. Case 8, that of Mrs. E. H., is rather remarkable in that the patient had had severe laryngitis for seven months in 1944, but with the use of penicillin spray her recovery was almost complete in seventy-two hours. Case 9, Mrs. W. H. shows the effect of the treatment on moderately severe laryngitis in a woman aged 74 with the history of severe pneumonia in 1941. Case 10, that of Mrs. A. L., suggests great help for puerperal women with colds, in whom coughing causes severe pain in the perineum. In 1 other case a severe cold in a pregnant woman a week before term was also treated successfully; this woman had had a mild form of pneumonia three weeks previously which had been treated with sulfadiazine.

CASE 8.—*History.*—Mrs. W. H., a white widow aged 74, weighed 190 pounds (86 Kg.). In 1941 she had severe pneumonia with auricular fibrillation, and when first seen on the third day of her illness she was almost dying; however, she recovered following the administration of sulfathiazole and digitalis intravenously. In the evening of Feb. 15, 1946 she had a temperature of 100 F. with chilliness and headache, and movements of her eyes were painful. These symptoms continued and on February 18 there developed a hoarse, painful, nonproductive cough which became progressively worse and more frequent. On February 19 she could only whisper hoarsely. She had not taken anything except fluids for four days.

Examination.—Examination revealed an obese woman with a flushed face and shining eyes who looked toxic. Her cough was frequent and irritating. The temperature was 100.6 F., the pulse rate 104 and the respiratory rate 22. The voice was only a hoarse whisper; the throat was moderately injected. In the chest there were a few rhonchi only, otherwise it was clear.

Treatment.—Penicillin spray was given, 40,000 units in twenty-four hours for two days, or a total of 80,000 units. The patient refused to take more penicillin because she was "cured" and "didn't want to waste it."

Course.—On February 20 (twenty-four hours after beginning treatment), the temperature was normal all day and the cough was loose, infrequent and painless, the headache was gone and the voice was better. The cough began to grow loose and painless within six hours after beginning to use penicillin spray. Her voice began to return sixteen hours after starting treatment and was normal in thirty-six hours. Her headache disappeared, and her eyes were better. There was no relapse.

CASE 9.—*History.*—Mrs. E. H. was a white woman aged 48. In 1944 she had a severe laryngitis which lasted for seven months, at which time her disease was suspected of being tuberculous. Thorough investigation by roentgen ray and consultations with specialists ruled out this factor. Throughout the winter of 1945 she had a cough. On Jan. 29, 1946 a cough and generalized aching with nausea and abdominal soreness developed. These symptoms became progressively worse, and on January 29 her voice became a whisper. On January 31 her sputum was blood-streaked, but there has been no streaking since.

Examination.—On February 1 the temperature was 99 F. and the pulse rate 80. The patient was an obese woman with bright eyes and a flushed face; her voice was a husky whisper. Examination of her lungs revealed dulness with diminished breath sounds for a handbreadth at both apexes and bases, but there were no rales. The diagnosis was laryngitis of seventy-two hours' duration as a complication of influenza.

Treatment.—Penicillin spray was given in a dosage of 40,000 units each twenty-four hours for four days, to a total of 160,000 units.

Course.—In six hours the nausea ceased. On February 3 (after eighteen hours of treatment) the patient's appetite had returned, the cough was loose, the sputum was mucopurulent and the pains were relieved. On February 4 (after forty-two hours), her voice was beginning to return and the cough was loose and infrequent. By February 5 the voice was normal and the patient felt almost well in every respect. There was no relapse.

CASE 10.—*History.*—Mrs. A. L., a married white woman aged 26, was beginning labor and had had a cold for forty-eight hours with a husky voice for eight hours.

Examination.—The temperature was 99 F. and the pulse rate 90. The patient was a pale, thin woman whose voice was moderately husky; her nose was running and her cough was frequent.

Treatment and Course.—In treatment of the laryngitis, penicillin spray was given in a dosage of 20,000 units daily for two days, a total of 40,000 units. All the symptoms of laryngitis disappeared in thirty-six hours, puerperium was normal and not complicated by a cough, which is always painful at such a time.

Postoperative Atelectasis.—The following case is reported not in proof of anything but as a suggestion that penicillin may be of help in postoperative atelectasis. One of the most striking effects of penicillin spray is that it loosens up and diminishes the frequency of a cough. This effect together with the encouragement of deep breathing and the prevention of the spread of a respiratory infection should be very helpful.

CASE 11.—*History.*—A. Fitz R., a married white man aged 28, was a veteran of the 1939-1945 war. During a typical attack of appendicitis, an appendectomy was performed through a transverse (Gurd) incision. The appendix was acutely inflamed but unruptured. Since 1942 the patient had always had a "smokers" cough, but preoperatively the chest was clear. Several army roentgenograms had been clear, the last in November 1945. Thirty-six hours postoperatively he began to cough frequently and to expectorate a small amount of thick mucopurulent sputum. There was also pain in the lower axillary region on the left side. There was no cyanosis. The temperature rose from 99 to 100.2 F. and the pulse rate from 88 to 100.

Examination.—For a handbreadth at the base of the left lung there were absent breath sounds, diminished vocal resonance and a dull percussion note. There was no friction rub and no demonstrable shift of the mediastinum.

Treatment and Course.—A dose of 40,000 units of penicillin as a spray was given daily for three days. In twelve hours, the cough was loose and much less frequent. The pain had gone. In twenty-four hours breath sounds were present in affected area, although diminished. In forty-eight hours the patient felt well again, and continued improvement was observed in the chest. In seventy-two hours he was apparently back to normal.

Comment.—Admittedly this was a mild atelectasis, but it is believed to be worth reporting because of the possibilities of penicillin spray as a help in postoperative care.

Blockage of Eustachian Tube.—Aerosol penicillin was used in 1 case of blockage of the eustachian tube.

CASE 12.—*History.*—J. W. C. was a white, married business man aged 56. Since Jan. 25, 1946 this man had buzzing, crackling sounds in his left ear after a mild head cold which began January 18. He had no fever or earache at any time.

Treatment and Course.—From January 25 to 28 he was given glycerine ear drops and ephedrine nose drops without relief. On January 28 these medicaments were discontinued, and he was told to spray his nose and throat with 14,000 units of penicillin in twenty-four hours; on January 29 this dosage was repeated. Within twelve hours after beginning penicillin therapy his disease was relieved, and it has not returned in the three weeks which have elapsed. Apparently a slight pharyngeal infection causing partial blockage of the eustachian tube was cleared up by the aerosol penicillin.

SUMMARIZED REPORT OF FOURTEEN ADDITIONAL CASES

Sinusitis.—There have been 2 cases of sinusitis on which this aerosol method of treatment has been efficient, and my confrères in this area also have reported success with penicillin spray in several cases. When sinusitis alone is present forced breathing is not desirable, and it is well to increase the frequency of the doses from the usual four hours to two hours. The pause between inspiration and expiration is important in this disease to permit the penicillin to settle on the mucous membranes.

Influenza.—It must be remembered that most of the cases reported previously herein began as influenza, and became complicated; they are grouped and reported under the diagnosis of that complication, such as pneumonia, laryngitis and the like. In the majority of the additional cases to be summarized under the title of influenza, the patients had tracheobronchitis. In 12 cases of uncomplicated influenza, or tracheobronchitis, the patients were treated with penicillin spray. Nine of them had a temperature of about 101 F., and all appeared toxic, with flushed faces and shining eyes. All had an annoying, frequent, painful, nonproductive cough, and 3 had nausea as well. Their disease was the type that often develops into full-blown pneumonia. The patients were apprehensive and restless, due to the racking cough as well as to the toxicity. Following treatment with penicillin spray, the cough became less frequent and less painful in four or five hours. If it were not greatly relieved in twelve hours, one could be sure that penicillin was not being taken as directed. The temperature fell 1 or 2 degrees Fahrenheit in the first twelve hours and by thirty-six hours was about normal. The most striking features in the treatment of these patients with penicillin were the relief of the irritating, painful cough and the attainment of a sense of well-being and a general improvement.

Two patients when first seen were dragging around "after getting over the flu." They were pale, weak, perspired easily and were bothered by a "tight" cough. They both responded well to 40,000 units of aerosol penicillin daily for three days, which apparently cleared up their residual infection.

In 1 case a physician, overworked and continually exposed to influenza, as well as to bad winter roads, was treated early. Within a few hours of having generalized aching, a headache, a raw throat and chilliness, penicillin therapy was begun with a dosage of 40,000 units in twenty-four hours and continued in this amount daily for three days. His temperature never went higher than 99 F. (it was elevated for twelve hours only), and he was able to carry on his work throughout, without feeling sick longer than that twelve hours. This patient carried the atomizer in his car. He had had to spend four to seven days in bed with the influenza each winter since 1931 and had been certain, from his symptoms, that he would have to do so this time. Several other patients expressed the opinion that: "This is the easiest time I ever had with the flu, it always used to last so long."

Unsuccessful Therapy.—There were 2 failures in this series of 26 cases of treatment with aerosol penicillin. Both were in elderly ladies over 70 years of age with fixed ideas. They had great faith in sulfa drugs as a result of previous favorable experiences, and both were anxious to have sulfa drugs again. One had chronic bronchitis of thirty-four years' duration and the other had had chronic cholecystitis for fifteen years. The indication for penicillin was to prevent pneumonia. Following penicillin spray, both complained of nausea and the patient with cholecystitis had vomiting as well. In 1 patient the nausea was helped by giving the spray every hour, while in the other the drug was discontinued after twelve hours, with no effect on the vomiting. One subsequently reacted to sulfadiazine therapy, while the other carried on slowly with an astounding series of poultices and patent medicines, but went on to a spontaneous cure in spite of all the medicaments. The patient with cholecystitis always vomited after taking any medicine.

SUMMARY AND CONCLUSIONS

Observations on this series of 25 cases suggest that the use of penicillin spray produced by a hand atomizer is effective against various respiratory infections. The method is easy, inexpensive and quite as generally applicable as sulfonamide therapy, yet it is not dangerous. Other series of cases using atomizers powered by oxygen under pressure have proved that penicillin spray is strikingly effective against pneumonia, some cases of asthma, bronchiectasis and abscess of the lung and that an effective systemic concentration of the drug in the blood is maintained in this manner. No toxic effects have been observed. This series of cases warrants further trial in a larger number of cases. The most striking effect of aerosol penicillin is the lessening of cough, sputum and toxicity.

The following conclusions may be deduced from this series of cases:

1. Penicillin spray generated by a hand or bulb atomizer is an effective treatment in many respiratory infections, including those of the nasopharynx.

2. The use of penicillin spray generated by an atomizer is a cheap, safe, painless method which is generally applicable to home use by untrained personnel.

3. The use of penicillin spray generated by an atomizer has great possibilities as a preventive medicine.

4. Penicillin spray is far more effective than oral penicillin as used at present. It has been proved elsewhere that its use is more effective by inhalation than by injection against some respiratory infections.

5. The dosage of penicillin spray is not definitely determined, but in this series of cases, small doses proved efficient.

V 13
1946

ENURESIS, A PSYCHOLOGIC PROBLEM OF CHILDHOOD

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Enuresis, especially during sleep, is one of the commonest and most troublesome problems presented by patients during childhood. Because of it, parents seek the help of the physician in great emotional distress. Their distress is a compound of resentment because their child is incontinent, while they know of many others of equal or a much younger age who do not soil their beds; of shame lest this family skeleton come to the notice of their family and friends, and of fear that their child may be defective. Their resentment is all the greater if the child sometimes goes through a night unsoiled, because they are then fully convinced that only his individual manifestation that he is a member of a sinful and perverse generation stands between him and a dry bed at all times. Their fear that he will always be a bed wetter cannot be better described than in the words of the mother of a child just turned 2 years who was as yet unable to remain dry at night though he behaved in an unusually advanced manner when awake, when she said, "I can just see him still wetting his bed when he is 10 years old."

Unfortunately, many parents have not been taught the simple elementary fact that voluntary control of the act of urination during sleep arrives at a later age than during waking hours. Their failure to act in terms of this single bit of knowledge causes them to heap shame, their resentment, physical punishment, disagreeable dietary and medical and surgical treatment on a perfectly normal child.

Since this paper is limited to the discussion of enuresis as a psychologic problem, the assumption is made that every child who presents the symptom of enuresis will be carefully studied to rule out infection and, when necessary, anatomic abnormalities within the urinary system. Fortunately, the presence of infection can be readily detected by routine examination of the urine. Abnormalities of structure can also now be readily demonstrated by intravenous urography [1] and by retrograde pyelography when this further study is indicated. An unusually small meatus can be plainly seen in the male and accurately measured in the female with sounds. A history of being continuously wet, though able to urinate normally at intervals, points unmistakably to the presence of an ectopic ureter.[2]

Failure to secure satisfactory improvement after a fair trial of psychotherapeutic methods in which the parents have given full cooperation may indicate the need for roentgenographic studies on an apparently normal child. When a child has been free from enuresis for months or years and then relapses into it, organic disease must be carefully ruled out. Diabetes, nephritis, a history of or present infection within the urinary tract, and anatomic deformity which had previously given no sign or symptom must have due consideration as possibilities. Such conditions are far more rarely present than a relapse into an infantile stage of development by the child because of some conflict which seems to him to be otherwise insoluble.

Also, since the purpose of this paper is to suggest a method of teaching parents to understand their child's enuresis and so to enable them to help him overcome it, no attempt is made to present an extensive review of the literature on the subject. Many writers [3] have shown that enuresis is predominantly a psychosomatic problem, so no claim to originality of that concept is made. A clear conviction in my mind that, in the absence of demonstrable disease or deformity, enuresis is only a part of the behavior pattern of the individual has enabled me to "cure" a far greater number of patients than by the use of any one or all the other methods known to me.

The parents who are troubled by their child's enuresis are instructed as follows. No child should be accused of enuresis until he is well beyond the age at which he can fairly be expected to have well developed control of the function of micturition even when he is asleep. In all fields of learning there is wide variation in the speed at which normal persons acquire a given skill. No one questions that such common accomplishments as walking and speech become possible for normal children at widely variable age levels. Why, then, should there be such insistence that all children should be both intellectually and functionally capable of control of the bladder at a given age?

Control of the bladder, and of the bowel as well, passes through three stages:

The first stage, during early infancy, is largely reflex. During the earlier months there seems to be only slight awareness of the act. The infant urinates about every fifteen minutes, and an important part of the early education of the mother is to warn her specifically against any attempt to keep him dry.

In the second stage the intervals between urinating become longer, often being extended to one hour after the end of the first year. There is by this time a definite increase in the child's awareness of the act, but there is as yet little or no conscious control. Many children learn at about this age to urinate and defecate voluntarily when placed on the toilet seat. The ability to release the sphincters of the bladder and bowel may be perfected many months before the child can voluntarily inhibit their release. When this stage has become established, the mother must be carefully instructed that she is putting him on the toilet at regular intervals primarily to "catch" him, saving herself a disagreeable task, and that she is not training him. If undue emphasis is allowed to rest on the belief that she is training him, all failures will be laid at his door. The only contribution made to training by keeping the child clean is that he gradually learns to prefer it to being unclean.

Read before the Section on Pediatrics at the Ninety-Fifth Annual Session of the American Medical Association, San Francisco, July 3, 1946.

1. At the Children's Hospital of the East Bay (Oakland) the following method has been found to yield highly satisfactory results from intravenous urography for children of all ages: 1. The child enters the hospital the day before the study is made. 2. A colonic flush of warm water is given after admission and is repeated about two hours before the roentgenogram is taken. 3. Fluids by mouth are withheld for sixteen hours before the roentgenogram is taken. Breakfast is a dry meal. 4. Thirty to forty-five minutes before the roentgenogram neostigmine is given subcutaneously in the following doses: for infants and small children, 0.5 to 1 cc. of 1:4,000 solution of neostigmine methylsulfate (25 mg. per cubic centimeter), and for older children, 0.5 to 1 cc. of the same in 1:2,000 solution (50 mg. per cubic centimeter). 5. Neo-Iopax is given intravenously, to infants, 8 to 10 cc.; to children weighing 20 to 30 pounds (9.1 to 13.6 Kg.), 10 to 15 cc., and to older children, 15 to 20 cc. 6. Roentgenograms of the urinary tract are then taken at five, fifteen, thirty, forty-five and sixty minute intervals. If excretion is slow roentgenograms may be taken at two, three and four hour intervals.

2. Cristal, D., and Greene, L.: Urinary Incontinence, J. A. M. A. **130**: 1061 (April 20) 1946.

3. Kanner, L.: Psychopathology of Childhood, in Brennemann, J.: Practice of Pediatrics, Hagerstown, Md., W. F. Prior Company, Inc., 1945, vol. 4, chap. 13, p. 42. Aldrich, C. A., and Aldrich, M. M.: Babies Are Human Beings, New York, The Macmillan Company, 1938, p. 92. Gesell, A., and Ilg, F. L.: Feeding Behavior of Infants, Philadelphia, J. B. Lippincott Company, 1937, p. 164; Infant and Child in the Culture of Today, New York, Harper & Bros., 1943.

The first two stages are physiologic, while the third stage is psychologic. The second gradually merges into the third stage, which is distinguished by the gradual coming of the act of urination under conscious control. This last stage is added to the two preceding, natural ones with an awareness of time and place by the needs and conscious wishes of civilized man. Since this third stage is a self-imposed discipline, it can be taught and learned only when a child has grown and developed sufficiently to exercise some measure of conscious self control. McGraw [4] in her study of twins found the average age at which the child begins to assume this responsibility was 23 months and that trained and untrained twin siblings arrived at the goal almost simultaneously.

Enuresis continues beyond the age at which it should disappear because of one or any possible combination of three psychologic conditions in the child. The first reason or condition is that the child has not yet grown up with particular reference to control of the bladder. He may be unusually advanced in other ways, but this function has perhaps developed slowly. On the other hand, his ability to control this function may have fully developed even earlier than usual, but for some reason he has failed to acquire the ability to use it. Perhaps impatience, blame and punishment on the part of his parents have retarded progress, bewildered him and left him no tangible reason for cooperation. The second basis for continued enuresis is that subconsciously the child wishes to remain in or return to the protected, irresponsible state of infancy, rather than to assume the normal dangers and responsibilities for his age. The third reason, also purely psychologic, like the first two, is one in which subconscious resentment against his parents is dominant. Wetting the bed is his way of getting even with them for too constant criticism (parent pecking). Many of these children are forced to eat when they are not hungry and have their personal liberties otherwise needlessly interfered with.

Any one or a combination of the psychosomatic states just described may be the basis for continued enuresis. The treatment must therefore be reeducation of the parents and the child, rather than the use of any drug, change in diet or fluid intake or any surgical instrument. The very multiplicity of drugs for this purpose bespeaks their uselessness, although some that are given when the child is ready to abandon bed wetting as a method of behavior get unearned credit. Medical treatment, such as excess salt or deprivation of fluids, that is unpleasant, may cause an intelligent child to substitute some other infantile behavior in its place. The prospect of a second cystoscopic examination [5] or of having the periodic passage of sounds continued may cause enuresis to cease but leaves the child, at best, no further advanced in emotional growth and development.

Since the medical and surgical approach to the problem of enuresis seldom solves it, too great dependence on them may cause the habit to continue late into childhood or even into adult life. When this occurs the habit becomes more fixed, and self respect demands that its victim believes it to be unavoidable. With this belief there must be a lack of self confidence in his ability to act otherwise.

That enuresis is essentially a psychosomatic problem is borne out by the fact that girls seldom continue it after the menses are well established. The older textbooks taught that this cessation was due to the secretion of hormones peculiar to the menstrual function. On the contrary, it is due solely to the psychic change that comes to every girl at that time. "I'm a woman now and must begin putting away childish things." Boys have no such dramatic passage into manhood; but members of both sexes often discontinue enuresis overnight just before they marry.

SUMMARY

Enuresis is discussed as a psychosomatic problem and a method of instructing parents is outlined.

2940 Summit Street.

ABSTRACT OF DISCUSSION

DR. ERNST WOLFF, San Francisco: Dr. Sweet's analysis of enuresis as an essentially psychologic problem is convincing. His method of parental therapy is excellent. The parents are relieved of their feelings of hostility, anxiety and guilt by putting their child into the care of the physician who takes over their parental responsibility. The physician restores feelings of satisfaction in their offspring by testing and pronouncing their child to be physically normal. He changes the parents' hostility to friendliness because he is able to change their dejection into pride. This is accomplished by teaching the developmental history of urinary control. Dr. Sweet's theory that in such physical functions children train themselves and are not really trained by parents has been brought out by many examples of parents who deliberately refrain from ordinary practices of training or "breaking the child's habits" and yet are rewarded by satisfactory cooperation at the appropriate time. Indeed, if one regards bowel and bladder training as a part of the general educational activities of the parent one may point out that, in developmental matters, parents really do not educate. They either create conditions which allow children to develop to their full capacity for maturity or, by wrong attitudes, which they think are of educational value, they interfere with the optimal development. Dr. Sweet's first two stages, which he calls physiologic, are excellently described. The third stage, that of acquiring conscious control of urination, implies that the child also gains unconscious control while sleeping. Perhaps it is not accidental that urinary control is achieved at that point in the child's development in which the psychoanalytic school conceives of the personality structure as being complete. During the first stage of urinary control the baby is motivated only by primitive drives leading to basic physical gratification; the psychoanalysts call this the "id" stage. During the second half year the baby's "ego" is developing. The baby gains the capacity to perceive the world around him, to become conscious of his own wishes and to act with conscious will. This leads to increasing urinary control during the time of consciousness, namely the period of being awake. In describing the third stage, Dr. Sweet uses the words "improved discipline" and "responsibility." This denotes that the third driving power of personality in psychoanalytic thinking, namely conscience or "super ego," has emerged. It is actually not accidental that unconscious bladder control and the completion of personality structure emerge simultaneously and could not be expected earlier. It may be noted that in many normal children control is not achieved until after the fourth birthday. Dr. Sweet's analysis of the interferences with completion of the third stage are significant. I would differ with him only as far as the relation of conscious and unconscious forces of motivation are concerned.

DR. CLIFFORD D. SWEET, Oakland, Calif.: I thank Dr. Wolff for discussing my paper so ably. I should like to reemphasize one or two things that he mentioned. One is the change in relationship. In my relationship with the parents I try to make them feel that they are the child's teachers, the child's guardians, not the child's jailer, that punishment has no place in the bringing up of a child unless he transgresses a law. We want to

4. McGraw, M.: Neural Maturation as Exemplified in the Achievement of Bladder Control, J. Pediat. **16**: 580, 1940.
5. Brodney, M., and Robins, S.: Enuresis: The Use of Cystourethrography in Diagnosis, J. A. M. A. **126**: 1000 (Dec. 16) 1944.

V 13
1946

live under a law. So does a child. Sometimes when the parents ask me if they can spank a child I say "Yes, if he breaks a law which in family council has been passed; then, if his parents break it, they get the same treatment. Then I think it is all right to spank the child under the same circumstances." I think we must give particular emphasis to the idea that the child must not be too upset when he fails to keep himself dry. When a child is brought to you it is going to take time to straighten him out. We must emphasize that one of the common causes of human failure is the inability of the fellow to pick himself up and go on after he falls down. He may have done very well for months and if he fails once everybody says "You are no good" instead of encouraging and helping him to go on again. I think it is highly important that we do not consider the problem of enuresis on its own merits. It is only a part of a general behavior problem, and the method of treating it is to help the child grow up, to remove the causes of the child's resentment against his parent. One of my young friends asked yesterday what he was to do with a case because, after several visits with the parents, he could not find any conflict in the family. That child may well fall in a group that hasn't any real conflict but is still an infant and wants to remain an infant.

Clinical Notes, Suggestions and New Instruments

NEUROSYPHILITIC PATIENTS TREATED WITH PENICILLIN

Probable Herxheimer Reactions

HAROLD A. TUCKER, M.D.
and
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Baltimore

The penicillin treatment of syphilis is no longer entirely an inpatient experimental procedure. The practicing physician will be treating more and more patients with symptomatic and asymptomatic neurosyphilis. Two recent Herxheimer-like reactions of a neurologic character occurring in patients undergoing penicillin treatment of neurosyphilis at the Johns Hopkins Hospital were of such alarming proportions that it is thought wise to report them in some detail.

REPORT OF CASES

CASE 1.—A white woman aged 32, a housewife, was admitted to the ward on Aug. 1, 1945, because of aphasia and right-sided hemiparesis of two days' duration. She had been aphasic on two occasions within the previous ten months, but both times she had spontaneously recovered within a few hours. Hemiparesis had not been noted before. There was a history typical of dementia paralytica which dated back about ten months, but she had never been subject to convulsive seizures. She had had early syphilis when 19 years of age and had received an undetermined amount of treatment.

Examination on admission disclosed no evidence of meningeal irritation. She was capable of obeying commands but was aphasic, silly in her behavior and euphoric. The pupils were slightly irregular but responded promptly to light and in accommodation; the fundi appeared normal. The right arm and leg seemed stiff and she could exert no appreciable grip with her right hand. The palate was asymmetric, the left half being relaxed. Deep tendon reflexes were increased on the right side; the Babinski test produced dorsiflexion of the toes bilaterally. The titered serologic test for syphilis (Eagle modification of the serum flocculation test) was 64 units. The spinal fluid contained 27 cells per cubic millimeter and 66 mg. of protein per hundred cubic centimeters of fluid. The spinal fluid Wassermann reaction was positive with as little as 0.05 cc., and the colloidal mastic curve was 5555432100. Although gumma could not be ruled out with certainty, it was felt that a large area of softening due to dementia paralytica had occurred in the region of the left internal capsule adjacent to Broca's area.

At 6 o'clock on the evening of admission this patient was started on 50,000 Oxford units of sodium penicillin in isotonic solution of sodium chloride administered intramuscularly every three hours for two hundred doses to a total of 10 million units. During the next thirty hours there was no apparent change in her general condition except that the rectal temperature rose from 98.6 F. (37 C.) to 100.8 F. (38.3 C.) by midnight of the second hospital day. She ate a good breakfast unaided on August 3 but refused lunch at 11:30 a. m. At 11:50 a. m. the first of a prolonged series of convulsions suddenly developed. These were at first manifested by rapid clonic contractions of the facial musculature on the right side (excluding the muscles of mastication) as well as both extremities on that side. Positive plantar responses were elicited with very minor stimulation. Pupillary and extraocular movements were not abnormal at this time. She was not seen to swallow for over thirty minutes.

The patient was given large doses of anticonvulsant drugs, which controlled the activity to some extent. A suction apparatus was placed in readiness. Convulsions continued at intervals day and night about three to six times daily; each attack lasted several minutes or more and in one instance over an hour. When she was not actually convulsing she was capable of taking an adequately nourishing soft diet; after the first attack no further difficulty was noted with deglutition; she was not incontinent of urine or feces.

The character of the convulsions changed gradually; by Aug. 6, 1945, five days after the institution of penicillin therapy, spasm of the trapezius muscle on the right side and grinding of the teeth had become prominent observations. Ocular deviation to the right and nystagmus were noted, the rapid component of the latter being toward the left. The Babinski reaction was obtained only on the right side. Because there was no evidence of subsidence of convulsions, the drugs originally employed (morphine sulfate, atropine sulfate and barbiturate derivatives) were now superseded by isonipecaine (Demerol) and, later, isonipecaine and diphenylhydantoin sodium.

Convulsions were still occurring three to five times daily by August 13. Muscular weakness could now be demonstrated only in the right arm. Examination of spinal fluid obtained by a lumbar puncture at this time showed only 2 cells per cubic millimeter and 33 mg. of protein per hundred cubic centimeters. The Wassermann reaction was negative in dilutions higher than 0.2 cc., but the colloidal mastic curve was unchanged.

On August 17, fifteen days after the onset of convulsions, these motor manifestations ceased. Because her general nutrition had been well maintained the patient was soon ambulatory and was able to walk out of the ward unassisted when discharged on August 25. At that time she was oriented and had regained some speaking ability, although speech was slow and enunciation slurred. The uvula was in the midline. No sensory changes could be demonstrated, and only the left plantar response was abnormal.

This patient continued to improve clinically and serologically during a clinic follow-up period of over six months. She did her own housework, was able to come to the clinic alone and was neat in appearance, and her speech improved greatly. By two hundred and five days after the start of treatment the serologic titer of her blood had fallen to 8 Eagle units and an examination of the spinal fluid disclosed 1 cell per cubic millimeter and 13 mg. of protein per hundred cubic centimeters; the Wassermann reaction was positive with as little as 0.6 cc. and the colloidal mastic curve was 5432110000.

This patient probably had edema, inflammation or hemorrhage superimposed on a large area of cerebral softening associated with dementia paralytica, although the possibility of multiple or solitary gummas cannot be ruled out with certainty. The occurrence of the onset of convulsions less than forty-eight hours after the initiation of antibiotic treatment and during the febrile reaction, which is generally accepted as representing the com-

The work in this paper was done under a contract recommended by the Committee on Medical Research between the Office of Scientific Research and Development and the Johns Hopkins University School of Medicine and United States Public Health Service Venereal Disease Research and Post-Graduate Training Center.

monest Jarisch-Herxheimer phenomenon, suggests but does not prove a relationship. The point to be emphasized, however, is the possibility that convulsions in this case were a manifestation of the Herxheimer reaction.

CASE 2.—A Negro aged 30, a shipfitter, was admitted to the ward for penicillin treatment because examination of the spinal fluid obtained by a diagnostic lumbar puncture had disclosed 53 cells per cubic millimeter, 142 mg. of protein per hundred cubic centimeters and a colloidal mastic curve of 5555432100. The Wassermann reaction was positive with as little as 0.05 cc. of fluid. There was a history of chancre three years before followed by grossly inadequate treatment. He had remained objectively and subjectively well in the interim and had been seen in the clinic because of a positive routine blood test for syphilis. He had never suffered from epilepsy or "fits." Physical examination was entirely noncontributory. The Eagle titer of the blood was 16 units.

At noon on Dec. 12, 1945 he was started on a schedule of 50,000 Oxford units of sodium penicillin administered intramuscularly every three hours. At 8 o'clock that evening he had a rectal temperature of 102.6 F. (39.3 C.), which spontaneously subsided. It was noted that he seemed restless the following day but was not otherwise unusual in his behavior. That evening he was found on the floor, crying, moaning and throwing his body from side to side. He vomited several times during the night and was incontinent. Although he was completely disoriented he did not have patterned convulsions; aimless restlessness was the predominating observation. Large doses of sedative drugs were required to control the hyperactivity, and restraints were applied to all extremities. During that night his rectal temperature rose to 104.8 F. (40.3 C.) and was over 104 F. (40 C.) for at least two hours. It was felt that this entire picture represented an atypical Herxheimer reaction.

In spite of medication (paraldehyde, barbiturate derivatives) hypermotility was still present the following morning. Neck and hip signs of meningeal irritation were readily elicited, and the Babinski signs were obtained bilaterally. Under intravenous pentothal sodium anesthesia 0.5 Gm. a lumbar puncture was performed. The pressure was not abnormal and the fluid was clear. From the laboratory standpoint the only significant change from the one done two days before was a rise in cell count to 277 per cubic millimeter, of which 52 per cent were polymorphonuclear cells. Cultures of the spinal fluid were sterile. That afternoon he seemed better oriented and took fluids by mouth but was still incontinent both of urine and of feces.

Although sedation was still required, by December 15 there was less hyperactivity and he recognized visitors. At this time his speech seemed slurred, but as it became feasible to reduce the amount of sedative drugs this abnormality disappeared. At the time of discharge from the ward on Jan. 6, 1946, after he had received a total of 10 million Oxford units of penicillin, the cerebrospinal fluid contained only 30 cells per cubic millimeter and 57 mg. of protein per hundred cubic centimeters. The Wassermann reaction was positive with as little as 0.05 cc. and the colloidal mastic curve was 5555210000.

One week later he was reexamined. Neither physical nor formal psychiatric examinations gave evidence of abnormality, except that the Babinski signs were still obtained bilaterally.

The most recent examination was carried out seventy-two days after the initiation of therapy. Babinski signs were equivocal bilaterally. The Eagle titer of the blood was 4 units. The cerebrospinal fluid contained 6 cells per cubic millimeter and 26 mg. of protein per hundred cubic centimeters. The Wassermann reaction was positive in amounts of 0.1 to 1.0 cc. and the colloidal mastic curve was 5554221100.

At the time of the onset of this reaction the pleocytosis and positive Kernig and Brudzinski signs were suggestive of pyogenic meningitis. Acute syphilitic meningitis and a bizzare reaction to the lumbar puncture done two days before were also considered. Because of the temporal relation to the initiation of penicillin treatment and the associated febrile episode, a Jarisch-Herxheimer reaction was thought to be the most likely explanation.

COMMENT

From September to October 1943, when the Johns Hopkins Hospital group began the experimental study of the effect of penicillin on syphilis in all its forms, to the time of writing (Feb. 18, 1946) 208 neurosyphilitic patients have been treated with penicillin alone. Some reaction to the initiation of treatment was noted in 26.0 per cent (54 patients). The majority of those who manifested some type of reaction to treatment had only a slight elevation of temperature or transitory mental confusion or agitation lasting from one to several hours. In 2 patients receiving treatment for dementia paralytica, hallucinatory and paranoid trends became so extreme that it became necessary to commit both to institutional care after only one third to one half of the anticipated treatment (10 million Oxford units in twenty-five days) had been given. That penicillin was directly responsible could not be established, for exacerbations of paretic symptoms are known to occur following or during any type of treatment or without any known initiating factor.

The 2 cases presented in detail in this paper were distinctly unusual in that convulsions occurred during intramuscular injections of the antibiotic agent. Isolated instances of transverse myelitic symptoms and jacksonian convulsions lasting twelve hours have been noted elsewhere during the penicillin therapy of neurosyphilis;[1] presumably the intramuscular route was employed. Several reports[2] have been published clearly demonstrating that penicillin may cause irritative phenomena when given intracisternally, intraventricularly, intrathecally or by direct local application of concentrated solutions to the cerebral cortex. Increased respiratory and decreased pulse rates have been noted in man following intracisternal administration.[3] No signs of parenchymal or meningeal irritation were seen, however, after large intravenous injections in human beings in whom concentrations of penicillin in the cerebrospinal fluid were achieved as high as 0.55 Oxford unit per cubic centimeter.[4] Several investigators[5] have been unable to demonstrate significant amounts in the spinal fluid after massive intramuscular doses. It would seem unlikely, therefore, that the convulsions in the cases reported here were due to a direct irritative action of the antibiotic agent, especially when it is noted that seizures ceased although penicillin in full doses was administered on schedule throughout these untoward episodes. Although no proof is forthcoming that these were true Jarisch-Herxheimer reactions, their occurrence within the first forty-eight hours of penicillin administration associated with the febrile response generally accepted as the usual Herxheimer phenomenon makes this interpretation highly probable.

In the light of recent work on some fractions or derivatives of commercial penicillins, e. g. penicillins F, G, X, K and others less widely publicized, it has become apparent that demonstrable differences in specificity and activity occur. From the evidence at hand, the 2 patients who were the subject of this report received penicillin of "high purity" containing G, F and K in unknown proportions; it is probable that the predominant fraction was penicillin K.[6] To our knowledge no work has yet been done on the differences, if any, between these derivatives as regards the production of irritative phenomena in the central nervous systems of man or of laboratory animals.

1. Stokes, J. H.; Beerman, H., and Ingraham, N. R., Jr.: Modern Clinical Syphilology, ed. 3, Philadelphia, W. B. Saunders Company, 1944, p. 1267.

2. Russel, D. S., and Beck, D. J. K.: Local Action of Penicillin and Sulfamezathine and a Penicillin-Sulfamezathine Mixture on Rabbit Brain, Lancet **1:** 497, 1945. Walker, A. E., and Johnson, H. C.: Convulsive Factor in Commercial Penicillin, Arch. Surg. **50:** 69 (Feb.) 1945. Johnson, H. C., and Walker, A. E.: Intraventricular Penicillin: A Note of Warning, J. A. M. A. **127:** 217 (Jan. 27) 1945. Walker, A. E.; Johnson, H. C.; Case, T. J., and Kollros, J. J.: Convulsive Effects of Antibiotic Agents on the Cerebral Cortex, Science **103:** 116, 1946. Neymann, C. A.; Heilbrunn, G., and Youmans, G. P.: Experiments in the Treatment of Dementia Paralytica with Penicillin, J. A. M. A. **128:** 433 (June 9) 1945.

3. Abbott, K. H., and Vogel, P. J.: Successful Treatment of Posttraumatic Pneumococcic Meningitis with Large Doses of Penicillin, Bull. Los Angeles Neurol. Soc. **10:** 107, 1945.

4. Schwemlein, G. X.; Barton, R. L.; Bauer, T. J.; Loewe, L.; Bundesen, H. N., and Craig, R. M.: Penicillin in Spinal Fluid After Intravenous Administration, J. A. M. A. **130:** 340 (Feb. 9) 1946.

5. McDermott, W., and Nelson, R. A.: Transfer of Penicillin into Cerebrospinal Fluid Following Parenteral Administration, Am. J. Syph., Gonor. & Ven. Dis. **29:** 403, 1945. Macklin, T. J., cited by Schwemlein and others.[4]

6. Moore, J. E.: Personal communication to Dr. Tucker.

V 132
1946

Should such differences be demonstrated, it may be necessary to modify the opinions expressed in this paper.

The potential gravity of reactions such as these deserves emphasis. If bulbar paralysis had supervened in case 1, death might have occurred. In both, had the onset been elsewhere than in a hospital ward the results might have been equally disastrous. The possibility that such reactions may occur should be recognized by all physicians undertaking the treatment of neurosyphilitic patients with penicillin.

The Johns Hopkins Hospital.

Council on Physical Medicine

The Council on Physical Medicine has authorized publication of the following report. HOWARD A. CARTER, *Secretary.*

GENERAL ELECTRIC RS SUNLAMP ACCEPTABLE

Manufacturer: General Electric Company, Nela Park, Cleveland 12.

The General Electric RS Sunlamp generates biologically effective ultraviolet radiation for use in the home. According to the recommendations of the company, at a distance of 24 inches (61 cm.) the intensity of ultraviolet radiation is approximately twice that of the summer sunshine. At a distance of 36 inches (91 cm.) the intensity is about equal, and at a distance of 48 inches (118 cm.) it is approximately one fourth that of the summer sunshine. In other words, at a distance of 36 inches (91 cm.) from the sunlamp to the average untanned skin a minimum perceptible erythema will be produced in approximately fifteen minutes. An overexposure, as for example sleeping under it for several hours, may cause a serious and painful sunburn.

General Electric RS Sunlamp

The General Electric RS Sunlamp does not require a special fixture but can be screwed into any ordinary lighting socket energized by 110-125 volt alternating current source of electricity. Furthermore, a special reflector is not needed, since the upper part of the bulb is coated on the inside with highly polished aluminum. The lamp consumes 275 watts.

The RS sunlamp consists of a small quartz tube containing mercury vapor. This tube is connected in series with a tungsten filament to limit the amount of current that flows through the tube. Both tube and filament are enclosed in an outer bulb made of special transmitting glass for ultraviolet radiation. The polished aluminum collects and reflects forward most of the ultraviolet radiation generated by the passage of current through the mercury vapor in the quartz tube. When the lamp is first turned on, the filament lights up brightly just like an incandescent lamp. As the current heats the mercury vapor in the quartz tube, a small thermal (heat actuated) switch operates to put an additional length of filament in the circuit to limit the amount of current flowing through the quartz tube. When that happens, the lamp will flicker and the color of the light takes on a slightly bluish tinge owing to the light coming from the mercury arc. The lamp may blink on and off several times before it settles down to steady operation. When the lamp is turned off, it must cool several minutes before it can be relighted.

If the lamp is used on direct current circuits, its life may be very short. On alternating current circuits the life of the lamp depends on how it is used. The life depends not only on the total number of hours the lamp is burned but also on the number of times it is started. The average lamp is rated at 400 starts at twenty minutes burning each. Under average home use this rating has been found to give about two years' service. Some lamps will last longer and some less. In the sales contract the company arranges for a trade-in allowance to compensate the owner for the unused service in case the lamp burns out prematurely.

The ultraviolet output of the lamp gradually decreases throughout its life. This can be offset by increasing the exposure time or decreasing the exposure distance, or both. When a renewal bulb is secured, the exposure time should at first be decreased to avoid sunburn, as the initial ultraviolet intensity or strength of the new bulb may be considerably greater than that of the old one.

RS sunlamps may be burned in any position. They are equipped with a medium screw base and can therefore be used in any ordinary lighting socket, such as in a bridge lamp, in a ceiling socket, on a drop cord or in a portable lamp unit.

Electrical, physical and radiation characteristics of the lamp are as follows:

Watts	275 (combined mercury vapor arc and ballast)
Volts	110-125 (50-60 cycles A. C.)
Outer bulb designation	R-40
Material	Ultraviolet transmitting glass
Finish	Light inside frost-reflecting neck
Inner bulb	Quartz
Base	Medium screw
Maximum overall length	6⅞ inches (17.5 cm.)
Burning position	Any
Life	400 applications of 20 minutes each
Erythemal time	Approximately 5 minutes at 24 inches
Beam characteristics	40° divergence to 30% of axial intensity

Wavelength, Angstroms	Microwatts per cm² at 30 inches
3,129	120
3,022	38
2,967	15
2,925	(Intensity too
2,894	low to measure)
2,804	
2,753	

(For wavelengths 2,925 angstroms and shorter, the output is insignificant.)

Spectral measurements showed that in spectral quality and total intensity this lamp complies with the Council's requirements for acceptance of a "sunlamp."

The Council on Physical Medicine voted to include the General Electric RS Sunlamp in its list of accepted devices.

Council on Foods and Nutrition

PLAN FOR ACCEPTANCE OF JUICES

In order to stimulate interest in the production of fruit juices containing high natural levels of ascorbic acid (vitamin C), the Council on Foods and Nutrition recently decided to adopt a plan for the acceptance of juices in which effective conservation of vitamin C is evidenced by the presence of appreciable quantities of ascorbic acid in the juice at the time of packing. Minimum requirements for the ascorbic acid content which have been adopted by the Council are as follows:

Kind of Fruit	Mg. per 100 Cc.
Tomato	20
Grapefruit	35
Orange	40

Accepted brands are eligible for use of the Council seal.

FRUIT JUICE—TOMATO JUICE

Bercut-Richards Packing Company, Sacramento, Calif.

Sacramento Brand Tomato Juice meets the Council minimum standard of 20 mg. of ascorbic acid per hundred cubic centimeters at time of packing and has been granted permission to use the Council's seal on labels and in advertising with the following statement placed near the seal: "Meets Vitamin C Standard Adopted by the Council."

132
946

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SATURDAY, OCTOBER 5, 1946

THE PROBLEM OF PRESYMPTOMATIC CANCER

One method of attacking the problem of high cancer mortality, the second foremost cause of death, has been education of lay and medical persons to recognize the symptoms suggestive of early cancer. Periodic health examinations have also been advocated as a method of detecting early tumors, again with some success. At the same time the treatment of cancer has been improved, especially in external and accessible types, by refinements in surgery and irradiation. Ideas as to what constitute surgical accessibility have undergone gradual change, so that today every major area in the body is surgically accessible. The posterior mediastinum was one of the last to yield. Tumors may, however, still be inoperable and incurable because of their extent.

These methods attack the problem of symptomatic cancer—cancers which have symptoms. They leave untouched the important field of presymptomatic cancer, or cancer which is as yet symptomless, silent, latent or preclinical. Apparently some cancers are asymptomatic until they are incurable by methods of treatment now available. They may infiltrate widely or metastasize to distant sites before the first symptoms are noticed. Surgeons sometimes find inoperable tumors in persons who had symptoms for only a short time. Pathologists occasionally find at necropsy in persons who died of other causes a surgically inoperable tumor which had not produced recognized symptoms. Curability of cancer varies inversely with the duration of the disease; in early cases diagnosis and adequate treatment have most to offer, yet it is these tumors that are most likely to be symptomless.

The magnitude of this problem as a whole has not been determined, although some data can be found for individual types of tumors. Among the commoner types of cancer that may be silent until they are incurable are some of those that arise in the stomach, lymphatic system, outer part of the lung, body and tail of the pancreas, bones, gallbladder and liver. Some of the rarer types of cancer also may metastasize during their presymptomatic stage of growth.

Unless and until tumors can be prevented, presymptomatic cancer must be made recognizable if anything near full control of cancer is to be attained. Periodic examinations are excellent for detecting presymptomatic tumors in surface and accessible sites such as the uterine cervix, mammary gland, oral cavity and larynx. They are less helpful in the visceral tumors, where methods of diagnosis are time consuming, involve expense and require much highly skilled personnel. Perhaps it is asking too much to expect all older adults in the population to have x-ray examinations of the alimentary tract and other special diagnostic procedures several times each year. Some simple test with which the entire population could be periodically screened is highly desirable. Persons giving a suggestive reaction could then be studied further. Such tests for detecting tumors should be as simple as those for syphilis.

Many tests for cancer have already been devised. Some of them use chemical, immunologic or serologic technics. To date they have not attained wide acceptance because the errors, positive or negative or both, are too great. Efforts to find a test should not be relaxed because of failures in the past. While it may be too much to hope that some test may be discovered that will indicate which persons are potential cancer bearers, it is not unreasonable to believe that a simple method for detecting presymptomatic cancer cases will yet be discovered by an intensified and concerted effort.

V 132
1946

PENICILLIN AEROSOL THERAPY

Two principal arguments have been advanced to justify the administration of penicillin by inhalation: the difficulty and the cost of the intramuscular or intravenous methods and the possibility that there may be a more direct action of penicillin when this antibiotic is placed in more intimate contact with the infecting organism, as is the case when sprayed into the respiratory tract in the presence of respiratory infections. Several technics of nebulizing solutions containing penicillin have been employed. Vermilye,[1] for example, used an apparatus consisting of an oxygen tank equipped with a valve for controlling the flow of oxygen at about 4 liters per minute. The oxygen from this tank is allowed to flow through a Vaponephrin nebulizer by tubing attached to the intake arm. At some point in the rubber tubing a Y tube is inserted, leaving one arm of the Y free and the tube of the nebulizer open. Humphrey and Joules[2] studied two types of apparatus for producing a mist; one was a "Collison" inhaler, which is an instrument employing compressed

1. Vermilye, Herbert N.: Aerosol Penicillin in General Practice, J. A. M. A. **129**: 250 (Sept. 22) 1946.
2. Humphrey, J. H., and Joules, H.: Penicillin Inhalation in Pulmonary Disease, Lancet **2**: 221 (Aug. 17) 1946.

gas, usually oxygen. The other type was a Riddopag or a Rybar inhaler, both of which are worked by means of a rubber hand pump or by compressed air generated by a small electric pump. For administering penicillin aerosol in the treatment of sinusitis, Barach and his colleagues [3] employed a nebulizer with a rebreathing bag and cone shaped glass nose pieces for inhalation. A glass venturi tube inserted in the rubber tubing from the oxygen cylinder was also used to produce positive pressure by oxygen flowing through the distal end for negative pressure through the side arm. The purpose of employing this special technic was to determine the value of penicillin aerosol administered under negative pressure in the treatment of sinusitis. Elsewhere in this issue (page 272) Morse [4] describes a simpler technic in which the apparatus consists of a simple hand atomizer.

Up to now, penicillin aerosol has been employed in the treatment of a variety of infectious conditions of the respiratory tract.[5] Unfortunately the number of patients in each disease category is not impressive. Humphrey and Joules employed penicillin inhalations in the treatment of 80 patients with chronic pulmonary infections. Their group included chronic bronchitis, bronchiectasis, "respiratory infection and congestive heart failure," pneumonia and generalized bronchitis, lung abscess, suppurative pneumonitis, silicosis and bronchitis and atypical pneumonia. Of this group, 46 were improved and 17 were moderately improved. Southwell,[6] using four nebulizers in all of which the mist was delivered by oxygen pressure and conducted by wide tubing to a B. L. B. mask, treated 43 patients with bronchiectasis, bronchitis or asthma. He employed calcium penicillin in a saline solution in a strength of 25,000 units per cubic centimeter. Patients were given 100,000 units at each session, the inhalations lasting about thirty minutes with the oxygen flow at 8 liters per minute. A treatment course consisted in the administration of 1,000,000 units of calcium penicillin in ten consecutive sessions given two or three times daily. None of the patients with bronchiectasis treated in this manner showed improvement. Of 6 patients with bronchitis of short duration, 5 appeared to be cured and 1 was much improved. There were 5 patients with chronic suppurative bronchitis, none of whom showed improvement. All 5 patients with chronic nonsuppurative bronchitis were improved but none were reported as cured. Of 17 patients with "chronic bronchitic asthma" 1 was considered cured, 13 were improved and 3 showed no improvement. Four patients with allergic asthma were treated without evidence of improvement.

Barach and his group reported the results of 122 courses of therapy given to 110 patients with sinusitis treated with penicillin aerosol and negative pressure. Thirty-nine of the patients showed considerable improvement, 43 moderate improvement; slight improvement was noted in 17 and no evidence of improvement was found in 23.

In the paper by Morse, published elsewhere in this issue, a variety of respiratory conditions were treated with what is probably the simplest technic thus far employed. The results recorded are encouraging. However, much more needs to be done on the subject of penicillin administration by inhalation before this procedure can be considered of established scientific merit. Controlled studies are necessary. Large enough numbers of patients with a single respiratory disease need to be studied and compared with similar groups treated without penicillin and with penicillin administered by the usual intramuscular route. Comparative studies should be made on the value and accuracy of the various types of nebulizers and on their effectiveness in delivering the penicillin where it will do the most good. Important also are careful studies on the optimum dosage of penicillin when given by spray, the preferred frequency of administration and the most desirable medium for dissolving the penicillin. Until these and similar questions have been settled, the administration of penicillin by inhalation for respiratory infections will remain empirical.

3. Barach, Alvan L., and others: Penicillin Aerosol and Negative Pressure in the Treatment of Sinusitis, Am. J. Med. **1**: 268 (Sept.) 1946.

4. Morse, Frank W.: Penicillin Spray by Bulb Atomizer in Respiratory Infections, J. A. M. A. **132**: 272 (Sept. 28) 1946.

5. Segal, Maurice S., and Ryder, Claire MacIntyre: Penicillin Aerosolization in the Treatment of Serious Respiratory Infections: A Preliminary Report, New England J. Med. **233**: 747 (Dec. 20) 1945.

6. Southwell, Neville: Inhaled Penicillin in Bronchial Infections, Lancet **2**: 225 (Aug. 17) 1946.

CAPACITY OF THE PULMONARY ARTERIES AND VEINS

Macklin [1] calls attention to the fact that the blood vessels in the normal lung are uniquely situated in that they are surrounded by expanding and contracting air spaces and that this environment influences their behavior, causing with each respiratory cycle a rhythmic increase and decrease. In inspiration the arteries and veins become elongated and widened by the traction of the stroma connecting their walls with the enveloping air spaces, while in expiration these vessels undergo a shortening and narrowing by reason of the recoil of their specialized elastic fibers. Thus in respiration their content of blood is increased and in expiration it is decreased. This action is regarded as a sort of auxiliary hemic pump or pulmonary "accessory heart" whose role is most striking in the vigorously exercised body of the healthy youthful person or animal. To support these views Macklin offers x-ray evidence consisting of the arterial and venous shadows of collapse and moderate inflation in two equivalent lungs. One set of experiments consisted in transecting the abdomi-

1. Macklin, C. C.: Evidences of Increase in the Capacity of the Pulmonary Arteries and Veins of Dogs, Cats and Rabbits During Inflation of the Freshly Excised Lung, Rev. canad. de biol. **5**: 199, 1946.

nal aorta in a rabbit to promote free hemorrhage, after which the diaphragm was nicked to allow the lung to collapse, while in another animal the thorax remained unopened. The pulmonary vessels were immediately perfused with 0.4 per cent sodium nitrite and 0.5 per cent sodium chloride through a cannula in the inferior vena cava below the diaphragm. Radiopaque synthetic latex was now injected by gentle pressure on a syringe fitted into the same cannula. Fixation of the tissues and coagulation of the latex were then accomplished by 95 per cent ethyl alcohol containing 5 per cent of glacial acetic acid introduced into the trachea at low pressure and allowed to act for a day. The lungs, one collapsed and the other moderately inflated, were removed and found to be fairly pliable so that their lobes could be spread out for x-raying. The resulting prints show that the arterial shadows of the moderately inflated state in corresponding vessels are considerably longer and wider than those of the collapsed state.

Another set of experiments was carried out to show comparison of the arterial and venous shadows of collapse and moderate inflation in the same lung injected extrathoracically. In these experiments the blood vessels were washed out with the lung in the intact thorax. After careful removal of the lungs the hilus was clamped to prevent air from entering the blood vessels. A glass cannula was then tied into the pulmonary artery for the injection of the pulmonary arterial tree or into the left atrioventricular ring if the venous tree was to be injected. Each cannula was affixed to a reservoir containing the radiopaque fluid. An x-ray film of the vessels of the collapsed lung was thereupon made. Immediately after the lung was carefully inflated and during this process the radiopaque fluid in the reservoir was able to flow freely into the enlarging vessels. It was found that the operation of inflation gave added capacity to the arteries and veins, so that more fluid was admitted. When a state of moderate inflation was reached another x-ray film was made with the various lobes disposed in the same way as for the picture of the collapsed state, so that direct comparisons of the two contrasting phases in corresponding vascular channels could be made. These prove that the blood vessels have lengthened and for the most part widened during inflation. The form and size of the shadow of the inflated condition strikingly indicated an augmentation in volume of the pulmonary arterial system. The pulmonary veins behave like the arteries by lengthening and widening during inflation. Volumetric evidence of the capacity changes in the pulmonary arteries and veins during inflation and deflation was obtained by attaching two glass tubes or burets either to the left atrioventricular ring or to a cannula in the pulmonary artery.

The increase and decrease in the capacity of the blood vessels are caused by the air pressure within the air sacs. The ultimate source of energy in the living condition is to be found in the musculature of the chest wall and diaphragm, which periodically lowers the pressure within the thorax so that the surrounding air has a pressure advantage and flows into the lung, distending the air sacs and elongating and widening the blood vessels as well as their channels. The heart responds to the advantage of enlarged vascular capacity by beating faster and increasing its output into the pulmonary vascular bed. The lung or, more properly, the pulmonary vasculature may therefore be regarded, according to the author, as a bridge for the blood which must be crossed by sufficient amounts if the systemic vessels are to be properly supplied. This ability on the part of the lesser circulation to adapt itself to the greatly widened demands of violent, prolonged physical exercise is bound up with its investment of continuously expanding and contracting air sacs and with its innate distensibility and contractility. Viewed from this angle the pulmonary vasculature may be regarded as the pulmonic "accessory heart."

Current Comment

EXCHANGE OF STUDENTS

Legislation sponsored by Senator Fulbright of Arkansas and approved by the President August 1 authorizes the Department of State to use some of the funds from the sale of surplus property abroad for exchanges of students and other educational activities. Up to $20,000,000 can be earmarked for educational exchanges with any country which buys surplus property; a maximum of $1,000,000 can be expended in each year in each country with which the Department of State has entered into an agreement. Such an agreement has already been consummated with Great Britain, which will provide $20,000,000 from the sale of surplus property for educational exchanges with the United Kingdom and the British colonies. Similar agreements are being negotiated with Australia, New Zealand, China, the Philippines, Burma, India, Iran, Iraq, Saudi Arabia, Turkey, Egypt, Greece, Italy, Austria, France, the Netherlands, Belgium and the Scandinavian countries. The Fulbright plan authorizes these types of educational activities: (1) American students can be given grants of foreign currencies to be used to pay the costs of higher education or research in foreign countries; (2) American professors can be given grants to give lectures in foreign institutions of higher learning; (3) foreign students can be given scholarships to study at American nondenominational institutions abroad, such as the American University at Beirut, Syria, and Robert College at Istanbul, Turkey, and (4) foreign students can be given funds to pay for their transportation to the United States to attend American institutions of higher learning but not to pay expenses within the United States. A Board of Foreign Scholarships will be appointed by the President to select student beneficiaries, the board to

V 132
1946

include representatives of the Office of Education, the U. S. Veterans Administration, state educational institutions and privately endowed institutions. Preference will be given to veterans of the first and second world wars, and in the selection of American students geographic distribution will be considered. It seems unlikely that any scholarships will be awarded for the 1946-1947 academic year, but the Department of State hopes that grants can be made in the spring of 1947 for the school year convening in the autumn of that year. To what extent the provisions of this new law will be utilized in the field of medicine is not clear at present. Perhaps, when the procedures have been worked out in detail, more definite regulations will become available.

CAROTENE AND VITAMIN A IN THE BODY

In plants, vitamin A potency follows closely the yellow-orange color of fruits and vegetables. Thus sweet potatoes, carrots and yellow turnips were active in curing vitamin A deficiency, whereas the white varieties were largely without effect. Soon the concept became established that the yellow plant pigments alpha, beta and gamma carotene and kryptoxanthine were precursors of vitamin A in the body and that the transformation of these hydrocarbons to the alcohol vitamin A took place in the liver. The latter conclusion rested on the observations of Olcott and McCann [1] that when liver tissue from vitamin A deficient rats was incubated with carotene, and the ultraviolet absorption spectrum of the brei was examined, there was evidence of the presence of vitamin A. These observations were both confirmed and denied in subsequent studies. Nevertheless the liver has been considered the site of change of carotene to vitamin A. Several older studies have shown that when carotene is administered parenterally the vitamin A content of the liver is not increased.[2] In a contribution to this subject, Deuel and his co-workers[3] demonstrate that, whereas carotene given by mouth is effective in combating vitamin A deficiency without evidence of accumulation in the liver, it has no effect in this situation when administered parenterally, although in the latter case there is active deposition of the pigment in the liver. Furthermore, it was shown that there is no destruction of carotene in the intestine. These observations not only raise the question with respect to the alleged part played by the liver in the change of the hydrocarbon pigment to vitamin A but also point to the intestinal wall as a possible site for this transformation. One needs only to recall the effective way in which the intestinal epithelium synthesizes fats from the products of enzyme hydrolysis of the fat in the food to concede that the foregoing explanation is reasonable. A sound concept of gastrointestinal physiology is the beginning of wisdom in nutrition. Deviations in absorption play an important part in clinical syndromes such as pellagra or pernicious anemia and in other nutritional deficiencies.

1. Olcott, H. S., and McCann, D. C.: Carotenase: The Transformation of Carotene to Vitamin A in Vitro, J. Biol. Chem. **94**: 185 (Nov.) 1931.
2. Rea, J., and Drummond, J.: Zur die Bildung von Vitamin A aus carotin im tierischen Organismus, Ztschr. f. Vitaminforsch. **41**: 177, 1932.
3. Sexton, E. L.; Mehl, J. W., and Deuel, H. J.: Studies in Carotenoid Metabolism: VI. The Relative Provitamin A Activity of Carotene When Introduced Orally and Parenterally in the Rat, J. Nutrition **31**: 299 (March 11) 1946.

ELECTRICAL TRANSCRIPTIONS "KEEPING YOUR BABY WELL"

The Section on Pediatrics in cooperation with the Bureau of Health Education has produced a series of fifteen electrically transcribed fifteen minute radio programs entitled "Keeping Your Baby Well." In these fifteen interviews twenty pediatricians selected by the officers of the section have been interviewed relating to material which they have submitted. The details will be found on page 289 of this issue of THE JOURNAL. This series of transcriptions is the fourteenth of the electrically transcribed radio programs prepared under the direction of the Bureau of Health Education. There is now available a total of one hundred and eighty programs which, when used consecutively once a week, will keep a medical society broadcasting without interruption for more than three years. By that time additional programs will be made available. More than four thousand local broadcasts on more than one hundred and twenty radio stations have been made from these transcriptions. They are available to any local medical society, health departments or other health agencies. Agencies other than medical societies should procure approval from the local medical society in order to borrow the transcriptions. There is no charge connected with the loan except the expense of express shipment to return the records.

OVARIAN TRANSPLANTATION

Successful transplantation of ovaries between dogs of different breed has been reported by Whitney,[1] director of the Veterinary Clinic, New Haven, Conn. Early unsuccessful experiments were carried out by Whitney and others without regard to the physiologic status of the dogs. Successful transfer was effected only when both the donor and the recipient were in estrus. In the successful transfers the donors were bloodhounds and the recipients foxhounds. After incision of the capsule the ovary was removed at the hilus and transferred to the capsule of the recipient, which was then closed with fine catgut sutures. After transfer, signs of estrus in the recipient decreased gradually over a period of four or five days. Estrus then recurred in full intensity and continued for a normal period of twenty days. Signs of a second estrus were observed forty-nine days after the start of the previous period in one foxhound and on the ninety-eighth day in another. These periods did not correspond with the recipients' previous history but represent a continuation of the donors' cycle. One of the dogs was killed seventy days after termination of the second estrus. On microscopic study the ovaries appeared normal except for a few necrotic blood vessels at the hilus. Vascularization otherwise was well advanced.

1. Whitney, Leon F.: Science **103**: 654 (May 24) 1946.

ORGANIZATION SECTION

Washington Letter

(From a Special Correspondent)

Sept. 30, 1946.

Medical Officers Exempt from Army's Step Up in Discharges of Officers

The War Department has announced a plan to speed up discharges of temporary officers, affecting about half of its 170,000 commissioned personnel, as an economy move and to obtain a completely volunteer officer corps. Under the new plan most officers who would not have returned to civilian life until June 30, 1947 will be allowed discharges by the end of this year. About 85,000 officers involved could remain in by volunteering for extra service. The 25,000 regular army officers are not affected; also exempt are certain specialists and medical officers and recent officer candidate school enrollees.

Discussion on Medical Application of use of Atomic Energy

Among the subjects slated for discussion by 2,000 members and guests of the District of Columbia Medical Society at the three day conference which opened today in the Hotel Statler was the medical application of atomic energy, surgical progress in the war and advances in cancer treatment. Capt. George M. Lyon, chief medical officer of the Bikini atomic bomb tests, lectured on atomic energy and future health. The meeting was one of the largest and most important medical conventions ever held in Washington, stated Theodore Wiprud, executive secretary.

Chief of Negro Office of Health Conducts Conference Program

Dr. Roscoe C. Brown, chief of the Office of Negro Health, U. S. Public Health Service, led public discussion of the role of the church, home, school and community and public health nurses in combating tuberculosis at a conference of Virginia county tuberculosis associations. Also on the program will be Dr. Paul Cornely, head of the department of public health, Howard University.

Share Ride Plan for Clinic Patients Worked Out

Mrs. Madge H. Langley, director of the Montgomery County Health Fund, has worked out a plan whereby Maryland motorists traveling daily to the District of Columbia participate in a share the ride program to aid county residents in need of outpatient treatment at Washington clinics. Most persons getting such treatment require orthopedic, optical or other types of care. The plan does not include patients with communicable diseases or persons acutely ill.

President Truman Pays Surprise Visit to Bethesda Naval Hospital

Once a familiar place to the late President Roosevelt, Bethesda Naval Medical Center was paid a surprise visit last week by President Truman, who was accompanied by Vice Admiral Ross T. McIntire, formerly personal physician to President Roosevelt, and Rear Admiral T. C. Anderson, hospital commandant. The President shook hands and conversed with hospitalized sailors during the hour and a half tour.

Nurse Caring for Patients with Poliomyelitis Stricken with Same Disease

U. S. Public Health Service figures reveal that the infantile paralysis epidemic is on the wane. To the present 17,204 reports of poliomyelitis have been received, while in 1944, the peak year for infantile paralysis cases since 1916, only 13,570 cases had been recorded at this time. Among the persons who contracted the disease in Washington was Rennie Wolfe, a senior cadet nurse in training at Garfield Hospital, on temporary transfer to the isolation ward for poliomyelitis victims at Children's Hospital. She was placed in the ward with the children she had been attending the past month, since the height of the epidemic. Her case was diagnosed as mild.

Army Opens Rehabilitation Center for Deaf at Forest Glen Hospital

Brig. Gen. George C. Beach Jr., head of the Army Medical Center and Walter Reed Hospital, reports that the rehabilitation center for the deaf and hard of hearing has been opened at the Forest Glen section of the hospital with seventy officers and enlisted personnel, including eight women as patients. The center will be under the direction of Major Henry C. Barnaby of Glen Cove, N. Y., who will be assisted by about fifty instructors and technicians. Designed as a special unit for hearing aids, lip reading and speech correction, the Aural Rehabilitation Center will accommodate 250 students.

Appeals Court Rules Urinalysis Tests Proper Evidence in Drunkenness Cases

The District of Columbia Municipal Court of Appeals has ruled that urinalysis tests are proper evidence in cases involving drunkenness. The accused had appealed on three grounds, that his constitutional rights as to search and seizure were abrogated by use of a urinalysis as evidence, that there was not sufficient evidence that the test had not been tampered with or changed, and that the specimen constituted compulsory self incrimination. The court ruled against all points but did not comment on whether a sample taken under compulsion can be used as evidence.

V 132
1946

Committee on American Health Resorts

The Committee on American Health Resorts has authorized publication of the following statement on the acceptance of The Homestead, Hot Springs, Va. A copy of the rules on which the Committee bases its action will be sent on request.

W. W. BAUER, M.D.

THE HOMESTEAD, HOT SPRINGS, VA., ACCEPTABLE FOR LISTING BY COMMITTEE ON AMERICAN HEALTH RESORTS

The Homestead, Hot Springs, Va., applied for listing by the Committee on American Health Resorts of the American Medical Association. The Committee has been furnished with all the information required under its rules, including copies of advertising and promotional material, and a report on an inspection by a Committee representative. The submitted information and the report indicate that the institution is operated in accordance with the rules of the Committee. The distribution of advertising material not in accordance with these rules has been discontinued.

The Committee on American Health Resorts is satisfied that The Homestead is being operated in accordance with the rules of the Committee and has placed this institution on the list of American Health Resorts complying with the Committee rules for a period of one year beginning Sept. 1, 1946. This listing may be continued for three year periods if the listed institution continues to comply with the rules.

Official Notes

ELECTRICAL TRANSCRIPTIONS "KEEPING YOUR BABY WELL"

The Bureau of Health Education announces the fourteenth series of electrical transcriptions available September 16 under the title "Keeping Your Baby Well."

These transcriptions, featuring interviews with twenty pediatricians selected by the officers of the Section on Pediatrics of the American Medical Association, include the following topics and speakers:

1. You and Your Baby, C. Anderson Aldrich, Rochester, Minn.
2. The Premature Baby, Julius H. Hess, Heyworth N. Sanford and A. H. Parmalee, Chicago.
3. Keeping Our Babies Well, Borden S. Veeder, St. Louis.
4. Breast Feeding Is Best, W. C. C. Cole, Detroit.
5. Artificial Feeding Can Be Good, Clara M. Davis, Winnetka, Ill., and Henry Gerstenberger, Cleveland.
6. Babies Who Fail to Gain, C. W. Burhans, Cleveland.
7. Overweight Babies, R. L. Kennedy, Rochester, Minn., and J. E. Gonce, Madison, Wis.
8. Vomiting and Diarrhea, M. K. Miller, South Bend, Ind., and F. C. Rodda, Minneapolis.
9. Vitamins, J. A. Bigler, Highland Park, Ill.
10. Allergy, Ben Z. Rappaport, Chicago.
11. Care of the Baby's Skin, W. L. Crawford, Rockford, Ill., and Abraham B. Schwartz, Milwaukee.
12. Tonsils In or Out, Stanley Gibson and George S. Livingston, Chicago.
13. Child Poisonings, John Aikman, Rochester, N. Y.

Each program is summarized by Dr. W. W. Bauer, Director of the Bureau of Health Education. Scripts are written and interviews conducted by Harriet H. Hester. Recordings are RCA Orthacoustic. Applications for loan of these transcriptions should be addressed to the Bureau of Health Education, 535 North Dearborn Street, Chicago 10. Complete listings of available transcriptions, including this series and others, will be furnished on application to the Bureau.

Woman's Auxiliary

OFFICERS OF WOMAN'S AUXILIARY TO THE AMERICAN MEDICAL ASSOCIATION

Following are the national officers, directors and chairmen of standing committees for 1946-1947 of the Woman's Auxiliary to the American Medical Association:

President, Mrs. Jesse D. Hamer, 1819 North Eleventh Avenue, Phoenix, Ariz.

President-Elect, Mrs. Eustace A. Allen, 18 Collier Road N.W., Atlanta, Ga.

Treasurer, Mrs. Harold F. Wahlquist, 129 West Forty-Eighth Street, Minneapolis.

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Third Vice President, Mrs. E. Arthur Underwood, 3725 Wuana Vista Drive, Vancouver, Wash.

Fourth Vice President, Mrs. John B. Helmick, 1207 Fairmont Avenue, Fairmont, W. Va.

Constitutional Secretary, Mrs. William Butler, 327 Briarwood Avenue S.E., Grand Rapids 6, Mich.

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Mrs. David W. Thomas, 112 West Main Street, Lock Haven, Pa.

Mrs. Luther H. Kice, 95 Brook Street, Garden City, L. I., N. Y.

Mrs. J. L. Stevens, 67 North Mulberry Road, Mansfield, Ohio.

Mrs. VanBuren Philpot, Holly Springs, Miss.

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Mrs. A. A. Herold, 1166 Louisiana Avenue, Shreveport, La.

Mrs. Ralph Eusden, 4360 Myrtle Avenue, Long Beach 7, Calif.

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Postwar Planning, Mrs. Rollo K. Packard, 4940 South East End Avenue, Chicago 15.

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SPECIAL COMMITTEE:

Historian, Mrs. Elmer L. Henderson, 87 Valley Road, Louisville, Ky.

Parliamentarian, Mrs. Clarence G. Goodwin, 4646 South Woodlawn Avenue, Chicago 15.

Coming Medical Meetings

American Academy of Allergy, New York, Nov. 25-27. Dr. Karl D. Figley, 316 Michigan St., Toledo 2, Ohio, Secretary.

American Academy of Ophthalmology and Otolaryngology, Chicago, Oct. 13-18. Dr. W. L. Benedict, 102 Second Ave. S.W., Rochester, Minn., Secretary.

American Academy of Pediatrics, Pittsburgh, Nov. 13-16. Dr. C. G. Grulee, 636 Church St., Evanston, Ill., Secretary.

American Association of Railway Surgeons, Chicago, Oct. 29-31. Dr. Raymond B. Kepner, 547 West Jackson Blvd., Chicago 6, Secretary.

American Clinical and Climatological Association, Hershey, Pa., Oct. 21-23. Dr. James Bordley III, Johns Hopkins Hospital, Baltimore 5, Secretary.

American Otorhinologic Society for the Advancement of Plastic and Reconstructive Surgery, New York, Nov. 14. Dr. Norman N. Smith, 291 Whitney Ave., New Haven 1, Conn., Secretary.

American Public Health Association, Cleveland, Nov. 12-14. Dr. R. M. Atwater, 1790 Broadway, New York 19, Executive Secretary.

Association of American Medical Colleges, Edgewater Park, Miss., Oct. 28-30. Dr. Fred C. Zapffe, 5 South Wabash Ave., Chicago, Secretary.

Association of Military Surgeons of the United States, Detroit, Oct. 9-11. Col. James M. Phalen, Army Medical Museum, Washington 25, D. C., Secretary.

Indiana State Medical Association, Indianapolis, Oct. 29-31. Mr. Ray E. Smith, 23 East Ohio St., Indianapolis 4, Secretary.

International College of Surgeons, United States Chapter, Detroit, Oct. 21-23. Dr. Louis J. Gariepy, 16401 Grand River Ave., Detroit 27, Secretary.

Inter-State Postgraduate Medical Association of North America, Cleveland, Oct. 15-18. Dr. Tom B. Throckmorton, 406 Sixth Ave., Des Moines, Iowa, Secretary.

Kansas City Southwest Clinical Society, Kansas City, Mo., Oct. 7-10. Dr. A. Lloyd Stockwell, 630 Shukert Bldg., Kansas City 6, Secretary.

National Society for the Prevention of Blindness, New York, Nov. 25-27. Mrs. Eleanor Brown Merrill, 1790 Broadway, New York 19, Executive Director.

North Pacific Pediatric Society, Vancouver, B. C., Oct. 19. Dr. A. B. Johnson, Cobb Bldg., Seattle 1, Secretary.

Omaha Mid-West Clinical Society, Omaha, Oct. 28-Nov. 1. Dr. Roy W. Fouts, 1036 Medical Arts Bldg., Omaha 2, Secretary.

Pacific Association of Railway Surgeons, San Francisco, Oct. 18-19. Dr. W. T. Cummins, 1400 Fell St., San Francisco 17, Secretary.

Pennsylvania, Medical Society of the State of, Philadelphia, Oct. 7-10. Dr. Walter F. Donaldson, 800 Penn Ave., Pittsburgh 22, Secretary.

Southern Medical Association, Miami, Fla., Nov. 4-7. Mr. C. P. Loranz, Empire Bldg., Birmingham 3, Ala., Secretary.

Southern Psychiatric Association, Richmond, Va., Oct. 7-8. Dr. Newdigate M. Owensby, 384 Peachtree St. N.E., Atlanta, Ga., Secretary.

Virginia, Medical Society of, Virginia Beach, Oct. 14-16. Miss Agnes V. Edwards, 1200 East Clay St., Richmond 19, Secretary.

Wisconsin, State Medical Society of, Milwaukee, Oct. 7-9. Mr. Charles H. Crownhart, 110 E. Main St., Madison 3, Secretary.

132
946

GOVERNMENT SERVICES

ARMY

CIVILIAN CONSULTANTS TO THE SECRETARY OF WAR

The appointment of prominent civilian physicians, surgeons and psychiatrists as consultants to the Secretary of War through the Surgeon General was announced September 12. This brings the number of civilian consultants in the Army Medical Department to more than 200. Of those announced at this time, 62 are surgeons, 29 physicians and 20 neuropsychiatrists.

Major Gen. Norman T. Kirk, Surgeon General of the Army, under whose direction the medical consultant program was initiated during the war, said the appointments are aimed at maintaining the highest standards of medical practice. The consultants will augment the army staff of doctors caring for soldier patients and evaluate, promote and improve, wherever possible, the quality of medical care given American soldiers. More consultants will be added as the program is expanded, General Kirk said. Most of the appointees were veterans of medical service during the past war and thoroughly familiar with administrative and professional technics employed in the Army's hospital system.

The consultants whose appointments were announced September 12 are:

INTERNAL MEDICINE

Francis R. Dieuaide, New York.
Yale Kneeland Jr., New York.
William S. Middleton, Madison, Wis.
Maurice C. Pincoffs, Baltimore.
Thomas H. Sternberg, Los Angeles.
Myles P. Baker, Brookline, Mass.
John B. McKee, Winchester, Va.
Paul Starr, Pasadena, Calif.
S. Marion Salley, Miami, Fla.
David R. Sacks, San Antonio, Texas.
Harold D. Warren, Brooklyn.
Monroe J. Romansky, Silver Spring, Md.
Garfield G. Duncan, Philadelphia.
Lester C. Feemer, El Paso, Texas.
Edgar Durbin, Denver.
James J. Waring, Denver.
Orlando B. Mayer, Columbia, S. C.
John J. Sampson, San Francisco.
William J. Kerr, San Francisco.
Robert M. Shelton, Pasadena, Calif.
James Bordley III, Baltimore.
Louis A. Zetzel, Boston.
Harry T. Harper Jr., Augusta, Ga.
Arthur C. Curtis, Ann Arbor, Mich.
Wallace M. Yater, Washington, D. C.
Andrew G. Prandoni, West Englewood, N. J.
Samuel Morrison, Baltimore.

PEDIATRICS

Edward Campion, San Rafael, Calif.
John M. Nelson, Denver.

NEUROPSYCHIATRY

CLINICAL PSYCHOLOGY

Max L. Hutt, Bronx, New York.
Mrs. Elizabeth H. Ross, Washington, D. C.

PSYCHIATRIC SOCIAL WORK

Malcolm J. Farrell, Waverly, Mass.
William H. Everts, New Rochelle, N. Y.
Nolan D. C. Lewis, New York.
Alfred O. Ludwig, Boston.
Oscar B. Markey, Shaker Heights, Ohio.
Ivan C. Berlien, Detroit.
Roscoe W. Cavell, Detroit.
Orthelo R. Langworthy, Baltimore.
David McK. Rioch, Rockville, Md.
Walter Freeman, Washington, D. C.
William A. Scott, Kalamazoo, Mich.
Harvey M. Cleckley, Augusta, Ga.
Clarence H. Goddard, Pasadena, Calif.
Karl M. Bowman, San Francisco.
Alexander Simon, San Francisco.
Charles D. Aring, San Francisco.
Richard E. Kepner, Kailua, Oahu.
Ralph B. Cloward, Honolulu, Hawaii.

SURGERY

GENERAL SURGERY

Fred W. Rankin, Lexington, Ky.
John A. Hardy, El Paso, Texas.
John D. Lamon Jr., Albuquerque, N. M.
Carleton Mathewson, San Francisco.
Joel W. Baker, Seattle.
Edward B. Speir, Seattle.
Siegfried F. Herrman, Tacoma, Wash.
Gordon K. Smith, Los Angeles.
Thomas W. Botsford, Brookline, Mass.
T. B. Quigley, Boston.
James W. Hubly, Battle Creek, Mich.
Russell L. Mustard, Battle Creek, Mich.
Richard A. Stiefel, Battle Creek, Mich.
George D. Lilly, Miami, Fla.
Amos R. Koontz, Baltimore.
Fred H. Miller, Dayton, Ohio.
William A. Farmer, Fayetteville, N. C.
John G. Lee, New York.
Benjamin W. Rawles, Richmond, Va.

ORTHOPEDIC SURGERY

Louis Breck, El Paso, Texas.
David N. Cameron, El Paso, Texas.
Leonard B. Barnard, Oakland, Calif.
Ira O. McLemore, Seattle.
Louis H. Edmunds, Seattle.
William H. Goering, Tacoma, Wash.
Robert W. King, Pasadena, Calif.
Steele F. Stewart, Honolulu, Hawaii.
Carl Berg, Washington, D. C.
Milton Cobey, Washington, D. C.
William J. Tobin, Washington, D. C.
W. W. Plummer, Buffalo.

NEUROSURGERY

Frank W. Lusignan, San Francisco.
James W. Watts, Washington, D. C.
Barnes Woodhall, Durham, N. C.

THORACIC SURGERY

Paul C. Samson, Oakland, Calif.

UROLOGY

Raleigh L. Davis, San Antonio, Texas.
Wickliff R. Curtis, El Paso, Texas.
Thomas E. Gibson, San Francisco.
William A. Sumner, San Francisco.
Burton L. Stewart, North Hollywood, Calif.
Lloyd G. Lewis, Washington, D. C.

OTOLOGY

Raymond T. Cathart, Butler, Pa.

PLASTIC SURGERY

Charles W. Tennison, San Antonio, Texas.
Truman G. Blocker Jr., Galveston, Texas.

ANESTHESIOLOGY

John W. Winter, San Antonio, Texas.

OBSTETRICS AND GYNECOLOGY

Francis A. Snidow, El Paso, Texas.
Richard D. Pettit, Pasadena, Calif.

EAR, NOSE AND THROAT

M. P. S. Spearman, El Paso, Texas.
Eugene S. Hopp, San Francisco.
Walter P. Work, San Francisco.
Fordyce A. H. Johnson, Pasadena, Calif.
William H. Jenkins, Washington, D. C.

X-RAY

Richard S. Harrison, Pasadena, Calif.
Wilbur O. Upson, Battle Creek, Mich.
Arthur C. Christie, Washington, D. C.
Aubrey O. Hampton, Washington, D. C.

OPHTHALMOLOGY

Grant Balding, Pasadena, Calif.
Paul L. Cusick, Detroit.
L. Connor Moss, Washington, D. C.
Frederick C. Cordes, San Francisco.
Max Fine, San Francisco.

RADIOLOGY

Edgar M. McPeak, Washington, D. C.

DEPUTY CHIEF OF OPERATIONS

Col. Eugene W. Billick, M. C., has been appointed deputy chief of operations in the Surgeon General's Office to succeed Col. Bryan C. T. Fenton, who has been assigned to the Brooke Army Medical Center, Fort Sam Houston, Texas. Colonel Billick graduated at the University of Pittsburgh Medical School after taking his premedical work at the University of Pennsylvania. He attended the Army Medical School and Medical Field Service School, Carlisle Barracks, Pennsylvania, served at the Walter Reed General Hospital at Colon Hospital, Panama Canal Zone, and then completed the two year course at the Command and General Staff School, Leavenworth, Kan. He graduated from the Army War College in 1939 and then became assistant to the department surgeon in the Philippine Islands. He went overseas to Cairo in 1943.

R. O. T. C. UNIT REESTABLISHED

The Surgeon General has requested Washington University School of Medicine, St. Louis, to reestablish an Officers Reserve Training Corps unit. It will begin this fall under the direction of Capt. Richard Yore, who graduated from Washington University in 1939 and received his M.D. degree from the School of Medicine in 1943. He interned at the City Hospital in New Haven, Conn., and went into the service in 1944. He was stationed at the Medical Fields Service School at Carlisle Barracks, Pa., and in 1945 went overseas, serving with the Sixty-Sixth Division in France.

Washington University is one of twenty-three medical schools throughout the United States which will have an R. O. T. C. unit.

FLIGHT NURSES

Thirteen officers of the Army Nurse Corps graduated from the Army Air Forces School of Aviation Medicine, Randolph Field, Texas, on August 16 as "flight nurses." The course for flight nurses extends over a period of nine weeks. This is divided into three phases of three weeks each. The first phase is a review of various military and medical subjects required of all military personnel. The second is concerned with material peculiar to air evacuation, and the third is occupied by actual evacuation flights within the Zone of the Interior.

V 132
1946

NAVY

NAVY AWARDS AND COMMENDATIONS

Rear Admiral John Harper

The Legion of Merit was recently awarded to Rear Admiral John Harper (MC), U.S.N., "for exceptionally meritorious conduct in the performance of outstanding services in the planning, development and establishment of the United States Naval Hospital, National Naval Medical Center, Bethesda, Md., from the outbreak of hostilities until Feb. 4, 1942 and as medical officer in command of this hospital from Feb. 5, 1942 to April 12, 1945. An executive of outstanding organizational ability," continues the citation, "Rear Admiral Harper rendered invaluable service in expediting the establishment of the National Naval Medical Center and in constructing the Naval Hospital and administering this vital activity following its transfer from Washington to the new location. He equipped and staffed the hospital in a minimum period of time to provide the highest standard of professional care and treatment in all specialties relating to the medical department, developing the facilities of his command in accordance with the needs of the rapidly expanding Navy, Marine Corps and Coast Guard. By his foresight, judgment, tireless efforts and conscientious devotion to the fulfilment of an important assignment Rear Admiral Harper contributed materially to the success of our war effort, and his conduct throughout reflects great credit on himself and the United States Naval Service." Dr. Harper graduated from the University of Pittsburgh School of Medicine in 1913 and entered the service May 17, 1916.

Captain Walter F. James

The Commendation Ribbon was recently awarded to Capt. Walter F. James (MC), U.S.N., "for excellent service in the line of his profession as senior medical officer of the U. S. S. *Kirey* from March 1 to Nov. 19, 1943. By his professional skill and devotion to duty" says the citation "he established and maintained high standards in the care and treatment of evacuated wounded and medical cases. By his knowledge and planning he contributed materially to the saving of many lives and the return of personnel to duty. His performance of duty was outstanding and his conduct was at all times in keeping with the highest traditions of the United States Naval Service." Dr. James graduated from the University of Illinois School of Medicine in 1927 and entered the service June 18, 1926.

Lieutenant Commander Martin S. Buehler

The bronze star was recently awarded by the commanding general, Headquarters XXIV Army Corps, to Lieut. Comdr. Martin S. Buehler (MC), U.S.N.R., for meritorious service in connection with military operations against the enemy in preparation for and during the Okinawa, Ryukyu Islands, campaign Feb. 3, 1945 to June 30, 1945. Dr. Buehler graduated from the University of Minnesota School of Medicine in 1939 and entered the service Jan. 5, 1942.

Lieutenant (jg) Everett M. Delabarre Jr.

The Bronze Star was recently awarded to Lieut. (jg) Everett M. Delabarre Jr., New York. The citation accompanying the award read, in part, "For meritorious service in connection with operations against the enemy while serving in a Marine infantry battalion on Okinawa Shima, Ryukyu Islands, June 18, 1945. . . ." Dr. Delabarre graduated from Columbia University College of Physicians and Surgeons in 1943 and entered the service Oct. 10, 1944.

Captain George Brackett Dowling

On advice of the First Lord of the Admiralty, the King of England has approved the honorary appointment of Capt. George Brackett Dowling (MC), U.S.N., as an Officer of the Military Division of the Order of the British Empire for distinguished service to the Allied cause. Dr. Dowling graduated from George Washington University School of Medicine in 1917 and entered the service Sept. 6, 1917.

Captain William F. E. Loftin

Capt. William F. E. Loftin (MC), U.S.N., has been authorized to wear the Navy Unit Commendation Ribbon by virtue of his service on the U. S. S. *Salt Lake City* during March 26, 1943. Dr. Loftin graduated from the University of Maryland School of Medicine in 1926 and entered the service June 22, 1928.

Captain Robert Lane Ware

Capt. Robert Lane Ware (MC), U.S.N., has been authorized to wear the Navy Unit Commendation Ribbon by virtue of his service on the U. S. S. *Denver* during the period Nov. 1 to 2, 1943. Dr. Ware graduated from Emory University School of Medicine in 1931 and entered the service June 25, 1931.

MISCELLANEOUS

NEW CHIEF OF ENTOMOLOGY AND PLANT QUARANTINE DIVISION

The U. S. Department of Agriculture has announced the appointment of Edward F. Knipling to head the Division of Insects Affecting Man and Animals in the Bureau of Entomology and Plant Quarantine, Agricultural Research Administration, effective September 15, to succeed Emory C. Cushing, who has resigned from government service.

Mr. Knipling has been connected with the bureau since 1931. He and his associates developed or adapted practically all insecticides, repellents and methods employed for their application that were used by the armed forces. The United States Typhus Commission Medal was awarded him for his share in these developments. The citation stated that "these studies, enlarging scientific knowledge, led to the effective use of DDT in the control of epidemic typhus. . . ."

DDT development as a mosquito control agent and MYL and DDT powders for the control of typhus-bearing lice as well as many other wartime developments which protected the health of men in the military service all originated from this bureau, the major part of the work being done at a single laboratory of this division. These developments together with the new repellents, including the combination of dimethyl phthalate Indalone and R-612, which proved to be so effective in the protection of troops against mites which transmit Japanese River typhus, and mosquitoes which carry malaria and dengue, now rapidly becoming so valuable during peacetime, were used extensively by the allied armies all over the world. They reduced diseases carried by insects to a point where they became a major factor in the successful prosecution of the war.

DRIVE FOR FUNDS FOR MEMORIAL TO NURSES

A nationwide drive for funds to erect a national memorial to nurses will be under way November 17. According to former announcements, the memorial will cost two million dollars and provide a home and service club in Washington, D. C., with sleeping accommodations for at least three hundred women. The memorial has been incorporated in the District of Columbia, making the property tax free and donations to the fund tax exempt. At a ceremony at General Eisenhower's quarters, Fort Myer, September 19, Field Marshal Montgomery, chief of the Imperial General Staff, British army, received a scroll signifying his honorary membership in the Nurses National Memorial.

Services will be held at Arlington National Cemetery in Washington, October 20, honoring the nurses who died in World War II. The speaker will be Hon. Robert P. Patterson, Secretary of War.

PHYSICIANS SEPARATED FROM SERVICE

ARMY MEDICAL CORPS OFFICERS RECOMMENDED FOR/OR RELIEVED FROM ACTIVE DUTY

Alabama

Enzor, Allen A.....Crestview

Arizona

Lewis, Donald B.....Tucson

California

Barnett, Clair B.....Cypress
Barrett, William G.....Burlingame
Brown, Raymond M.....Berkeley
Bruning, Edward F.....Balboa
Cheney, Garnett.....San Francisco
Condie, Robert S.....Palo Alto
Ellis, Robley N.....San Francisco
Feldman, Sanford E.....San Francisco
Gibbons, Joel M.....Santa Paula
Grady, Charles W.....Palo Alto
Harms, Herbert E.....Oakland
Jacobson, Leland C.....San Bernardino
Jing, Fred Q.....Fresno
Kobal, Arthur L.....Montebello
Laird, George J.....San Diego
Layton, Walter B. Jr.....San Francisco
Marturano, Frank P.....Long Beach
Overstreet, Edmund W.....San Francisco
Raymond, John R.....Fresno
Schneider, Maurice.....Los Angeles
Woo, Theresa T.....Burlingame

Colorado

Barfield, James J.....Colorado Springs
Koschalk, Joseph.....Brighton
O'Dea, Norman J.....Denver

Connecticut

Dorfman, Jacob.....Hartford
Giddings, James C.....New Haven
Gourlie, Howard W.....Thompsonville
Kelly, Colman J.....Old Greenwich
Lehndorff, Peter G.....New Haven
Liebow, Averill A.....Hamden
Neidlinger, William J.....Hartford
Sayers, Daniel O.....Waterbury
Thomas, Andrew H.....New Britain

District of Columbia

Altman, Harry E.....Washington
Bush, Richard D.....Washington
Goldberg, Herbert A.....Washington
Kessler, Israel.....Washington
Krucoff, Morris E.....Washington
Levatin, Paul.....Washington
Loftus, James M.....Washington

Florida

Andrews, Edson J.....Tallahassee
Byrd, Emmett E.....Lake City
Funk, Neil E.....St. Petersburg
Karaphillis, John T.....Tarpon Springs
Kimble, LeRoy R.....Titusville
Long, Martin H. Jr.....Jacksonville

Georgia

Johnson, John F.....Macon
Ketchum, Walter H. III.....Forsyth
Kolman, Isadore I.....Savannah
Little, Frank A.....Thomasville
Lott, Oscar H.....Savannah

Idaho

Balding, Laurence G.....Boise
Meyers, Isadore.....Boise

Illinois

Atlas, Donald H.....Chicago
Balding, Bruce N.....Elgin
Bernstein, Max M.....Chicago
Borin, George M.....Peoria
Bryant, Joe.....Chicago
Chase, John F.....Chicago
Clowers, Walter C.....Springfield
Conroy, Wilfred A.....Chicago
Dina, Salvatore.....Chicago

Illinois—Continued

Dolan, Larsandrew.....Chicago
Ehrlich, Joseph C.....Chicago
Entin, Oscar L.....Chicago
Fahey, Richard P.....Chicago
Feinberg, Louis.....Chicago
Fischer, Burnell.....Decatur
Galt, Raymond M.....Chicago
Givner, David.....Maywood
Glueckauf, Lewis G.....Chicago
Grudzien Stanley R.....Chicago
Heinrich, Jerome F.....Wilmette
Izzo, Joseph L.....Evanston
Kelly, Sylvester M.....Chicago
Knudson, Joel W.....Oak Park
Leeds, Milton F.....Chicago
Levinson, Benjamin J.....Chicago
Machlan, Harold F.....Hines
McLauthlin, Carl H.....Chicago
Marquardt, Gilbert H.....Chicago
Nicholas, Everett E.....River Forest
Platt, Samuel S.....Chicago
Presman, David.....Chicago
Rosenfels, Paul.....Chicago
Russell, Lyle W.....Tiskilwa
Ryder, Bruce I.....Henry
Shafer, Roger D.....Christopher
Sintzel, Alois R.....Belleville
Slama, George F.....Chicago
Wilson, Arthur D.....Carrollton
Zimmerman, Nathan.....Chicago

Indiana

Byrne, Robert J.....Bicknell
Finot, Philip H.....Indianapolis
Freed, Carl A.....Attica
Funk, Vance A. Jr.....Vincennes
Hoover, Peter B.....Boonville
Johnston, Edward E.....South Bend
Kattany, Edward C.....Indianapolis
Knoll, William.....Indianapolis
Masters, John B.....Indianapolis
Wright, Joseph W. Jr.....Indianapolis

Kentucky

Berg, Lawrence E.....Outwood
Coe, Walter S.....Erlanger
Dodson, Carlisle V.....Richelier
Kaplan, Martin Z.....Louisville
Merritt, Burch A.....Fancy Farm
Painter, Max E.....Glasgow
Stephenson, Joseph E.....Pikeville
Witt, William R.....Louisville

Maryland

Cohen, Harry.....Baltimore
Huebner, Klaus H.....Elkton
Hunt, Richard H.....Baltimore
Jones, Emmett L. Jr.....Cumberland
Koontz, Amos R.....Baltimore
Lowe, William C.....Baltimore
Menning, Joseph H.....Baltimore
Osborne, John C.....Baltimore
Traum, Aaron H.....Silver Spring
Vogel, Louis Jr.....Baltimore
Zepp, Edwin A.....Baltimore

Massachusetts

Berenson, Wyman.....Mattapan
Blanchard, Joseph.....Brookline
Culver, Perry J.....Boston
Dee, John F.....Indian Orchard
Fay, Kevin J.....Roxbury
Freedman, Edward P.....Westboro
Guidone, Erel L.....Medfield
Hebert, Roger D.....Chicopee
Kos, Clair M.....Boston
Latorella, John.....East Boston
McLaughlin, Laurence S.....Woburn
Paul, David M.....Boston
Quinn, George E. B.....Boston
Ross, Mathew.....Brookline
Wallwork, David W.....North Andover

Michigan

Andrews, Sherman E.....Kalamazoo
Andrina, John J.....Flint
Ballard, James H.....Detroit
Bennett, Robert C.....Detroit
Beyer, Damon P.....Clio
Broaddus, John O.....Detroit
Coucke, Henry O.....Birmingham
Deering, Robert J.....Ecorse
Fisher, James M.....Grosse Pointe
Fitts, Ralph L.....Grand Rapids
Fraser, Harvey E.....Detroit
Johnson, Elmer F.....Eloise
Kirtland, William B. Jr.....Detroit
Kohn, Arthur M.....Detroit
Kuhn, Henry H.....Detroit
Lilga, Harris V.....Petoskey
Lundberg, Einar A.....Detroit
McDowell, Douglas B.....West Branch
O'Brien, Charles E.....Dearborn
Paalman, Russell J.....Grand Rapids
Schmidt, Harry F.....Dearborn
Schug, Richard H.....Detroit
Van Zwaluwenberg, B. R...E. Gd. Rapids

Minnesota

Bentson, James H.....St. Paul
Blake, Allan J.....Hopkins
Feinberg, Philip.....South Minneapolis
Lenander, Mellvin E.....St. Peter
Sorensen, Roy W.....Pelican Rapids
Weisman, Sydney J.....Minneapolis
Whelan, Joseph L.....Chisholm

Missouri

Bess, George G.....St. Louis
Bettonville, Paul J. Jr...Richmond Hts.
Bickel, Vern T.....Lamar
Bieri, Earl J.....St. Louis
Blair, Vilray P. Jr.....Florissant
Clark, Kendall A.....Fulton
Correnti, Nicholas A.....St. Louis
Craig, Owen W.....St. Joseph
Forgrave, John R.....St. Joseph
Forsman, Waldo W. Jr.....St. Louis
Freeman, David M.....Kirksville
Goetsch, Carl.....St. Louis
Hager, Victor K.....St. Louis
Hall, Lee A.....St. Louis
Hamilton, Caldwell K.....Kirkwood
Herrmann, Arnold J.....St. Louis
Higgins, Robert F.....St. Louis
Hill, James N.....Kansas City
Hobbie, Wallace.....Kirksville
Hoelscher, Harold F.....Treloar
Lefkin, Philip.....Platte City
Lieberman, B. A., Jr.....Kansas City
McCall, Edwin L.....Brentwood
McDonald, Eugene F.....Jackson
Mezera, Raymond A.....St. Louis
Morton, Paul C.....Springfield
Schwartzman, Bernard...University City
Willoughby, Jean B.....Independence
Wheatly, William K.....Crystal City

Nebraska

Klabenes, Frank J.....Omaha
Loudon, James D.....Omaha
Tatelman, Maurice.....Omaha

New Jersey

Adelman, Nathan.....Newark
Alford, Ralph I.....Montclair
Bleich, Alan R.....Pennington
Bourgeois, George A. III....Jersey City
Caldarola, Thomas J....West New York
Crater, Kenneth E.....Bloomfield
Elgen, Louis A.....West Orange
Fishwick, Dwight B.....Glen Ridge
Goldstein, Henry.....Newark
Gourley, Robert D.....Tenneck
Hayes, Marjorie.....New Brunswick
Isen, Paul J.....Freehold

V 132
1946

PHYSICIANS SEPARATED FROM SERVICE

New Jersey—Continued

Kassel, Mortimer H.....Jersey City
Liva, Vinicio G.....Lyndhurst
McAuliffe, Vincent J.....Jersey City
Mancusi-Ungaro, Harold R.....Newark
Merves, Louis.....Camden
Nolke, Anthony C. Jr.....Westwood
Perry, Frank L.....Woodstown
Pomeranz, Raphael.....Newark
Rube, Joseph A.....Ridgewood
Schwartz, Jacob R.....Fair Lawn
Spaeth, Walter.....Ocean City
Sullivan, John E. Jr.....Arlington

New York

Ahrens, Edward H. Jr.....New York
Albrecht, Robert M.....Green Island
Alperin, Benjamin J.....Freeport, L. I.
Ament, Richard.....Buffalo
Baker, George A.....Kenmore
Berkett, George D.....New York
Bernhard, Robert.....Bronx
Bodon, George R.....Rochester
Boyd, James L.....Glen Cove
Burstein, Charles.....Mount Vernon
Campbell, Coburn A. L...Port Jefferson
Carman, William R.....Islip
Cayaves, Paul G.....New York
Coviello, Vincent J.....Bronx
Cramer, Joseph B.....Rochester
Damato, Michael W.....Brooklyn
D'Amico, Anthony F.....Brooklyn
Danish, Louis J.....Hollis, L. I.
Delagi, Edward F.....Bronx
De Lalla, Vincent J.....Utica
Donohue, John M.....Bayville
Dresner, Solomon.....New York
Egidio, Paul T.....Kew Gardens, L. I.
Ehrlich, Hilbert W.....Bronx
Eisert, Otto.....Batavia
Eldridge, Ernest B.....Tonawanda
Enders, Joseph B. Jr.....Syracuse
Engel, Jerome.....Ravena
Feldman, Philip M.....Brooklyn
Fernbach, Paul A.....Cheektowaga
Finnegan, John L.....Flushing
Fisher, Martin M.....Brooklyn
Fleming, Robert I.....Randolph
Flynn, Raymond A.....New York
Galluccio, Joseph R.....New York
Gantman, Jacob.....Bronx
Gluck, Samuel M...Middle Village, L. I.
Godwin, Richard H.....Rockville Centre
Goldgraben, Seymour.....New York
Goldsmith, Jacob.....Brooklyn
Grantz, Irwin A.....Brooklyn
Gray, Basil C.....Oneonta
Halpern, Harold J.....Brooklyn
Hammerman, Henry J.....Brooklyn
Hathaway, Haviland G.....Binghamton
Hellmann, Charles H.....New York
Herzog, Jacob O.....New York
Hillman, Joseph H.....New York
Hurewitz, Benjamin.....New York
Igloe, Max C.....Forest Hills
Jacobs, Irving L.....Flushing
Jacobson, Harold G.....New York City
Jarcho, Saul.....New York
Johnson, Eldridge W.....Greene
Kanner, George.....Brooklyn
Kaplan, Lawrence I.....Brooklyn
Keller, Walter.....Wadsworth
Kempler, Samuel L.....Newburgh
Koenig, Alfred D.....Ozone Pk., L. I.
Kogan, Manuel.....Brooklyn
Krakauer, Hans.....Boston
Kroop, Irving G.....Brooklyn
Larson, Swen L.....Elmira
Lawrence, Edgar A.....New York
Lesser, Albert.....New Hyde Park
Levenson, Carl.....New York
Levine, Samuel.....Cold Spring
Levy, Erwin.....New York
Liebowitz, Hirsch R.....Brooklyn

New York—Continued

Lord, John C. Jr.....New York
Love, Edward.....New York
McCown, Ila A.....New York
Mandel, William.....Brooklyn
Metz, Herman A.....New York
Moore, Edson E.....Buffalo
Nathanson, Morton.....New York
Nussbaum, Kurt.....Buffalo
Okoniewski, Frank L.....Auburn
Orlov, Harry L.....Bronx
Padykula, Stanley G.....Endicott
Perrine, Alfred T.....Long Island
Petrone, John C.....Suffern
Randall, Henry T.....New York
Raphael, Albert J.....Brooklyn
Ring, Alfred.....Jamaica
Robb, George P.....White Plaines
Rosenblum, Marcus P.....Bronx
Roth, Aaron.....Brooklyn
Salzman, Ferdinand A.....New York
Schloss, Walter A.....Flushing
Sherwin, Carl P. Jr.....Scarsdale
Sickenberger, Patrick G.....Brooklyn
Swan, Harold R.....Tuckahoe
Taylor, Reginald M.....New York
Ward, Charles E. Jr.....Yonkers
Will, George J.....Dobbs Ferry
Wishik, Julian L.....Flushing
Zippert, George J.....New York

North Carolina

Exum, William A.....Snow Hill
Johnston, Joseph B. Jr....Barium Spring

Ohio

Adan, Alan B.....Brecksville
Alperin, Leonard J....Cleveland Heights
Berry, Clyde W.....Wapakoneta
Blazewicz, Selim J.....Pomeroy
Counts, Richard I.....Chillicothe
Curtis, George H.....Cleveland
Dobkin, Arthur.....Akron
Fink, Abraham A.....Toledo
Gignac, Ralph M.....Dayton
Goodman, Julien M.....Cleveland
Hawk, Bray O.....Strasburg
Hellwig, Edward F.....Cleveland
Hoyt, Walter A., Jr.....Akron
Jaffa, Jack I.....Maple Hts.
Kesinger, Herbert F.....McArthur
Kirk, Robert C.....East Palestine
Lancione, Peter.....Bellaire
Leonard, Donald E.....Cuyahoga Falls
McCoy, Francis W.....Columbus
Mack, Joseph A.....Canton
Pischieri, Joseph V.....Shaker Heights
Schnitker, Maurice A.....Toledo
Steele, Wendell M.....Newark
Thompson, Nicholas J.....Norwalk

Oklahoma

Holt, Willard D.....Altus
Smith, Jackson A.....Norman

Oregon

Fowlks, Everill W.....Portland
Gandin, Morris M.....Portland
Hyman, Milton D.....Portland

Pennsylvania

Arnold, Clifford H.....Ardmore
Austin, George M. Jr.....Philadelphia
Billman, Howard G.....Mt. Carmel
Boyer, Frank R.....Bethlehem
Bronk, Theodore T.....Irwin
Budzelka, Theodore R.....Pittsburgh
Burger, Richard W.....Cokeburg
Chemycz, Joseph R.....Essington
Christopher, Frank G. Jr.....Smithton
Clark, John K.....Wynnewood
Cullen, Charles J.....Portage
Davis, C. Reginald.....Johnston
deDiego, Manuel.....Lancaster
Eisner, Clarence A.....Pittsburgh

Pennsylvania—Continued

Engelman, Frank E.....Pittsburgh
Ferderber, Murray B.....Pittsburgh
Foertsch, Frederick E. Jr....Philadelphia
Glauser, Jacob.....Philadelphia
Gomez, George L.....West Chester
Hershfield, David H.....Wilkes-Barre
Hess, Paul G.....Manheim
Highberger, Edward S.....Greensburg
Hulick, George S.....Aldan
Huntzberger, Samuel S...Sinking Spring
Jameson, Earle C. Jr.....Philadelphia
Kramer, Abraham.....Philadelphia
Krugh, Francis J.....Pittsburgh
Kuehn, Conrad A.....Pittsburgh
Levy, Jacob J.....Allentown
Lucente, Edward R.....Philadelphia
Lucke, Balduin H. E. W....Philadelphia
McGurl, Thomas J. Jr.....Minersville
Miller, Robert H.....Wilkinsburg
Moylan, Joseph D.....Scranton
Naugler, Walter E.....Wayne
Newman, John H.....Pittsburgh
Parris, Herman M.....Philadelphia
Rankin, Paul H.....Sharon
Schwartz, Reuben.....Philadelphia
Selkovits, Sidney C.....Aliquippa
Simmonds, Henry T. Jr.....Shamokin
Yoders, Robert H.....Templeton

South Dakota

Kittelson, Horace O.....Sioux Falls

Tennessee

Kantor, Milton.....Mountain Home
Layman, Robert P.....Knoxville
Lorenz, John E.....Chattanooga
Phillips, Walter A.....Arlington

Texas

Johnson, Bascom Jr.....El Paso
Long, William E.....Dallas

Virginia

Chitwood, James L.....Hillsville
Drewry, Patrick H. Jr.....Richmond
Ellerson, Edmund M.....Staunton
Kohn, Theodore.....Richmond
Raiford, Fletcher L.....Franklin
Schneider, Charles F.....Charlottesville
Shetter, George A.....Richmond
Singer, Solomon.....Jonesville

Washington

Feldman, Noah.....Walla Walla
Hodgson, Edward R.....Spokane
Kraabel, Austin B.....Seattle
Lasater, James H. Jr.....Seattle
Laughlin, Robert C.....North Seattle
Watson, John A. Jr.....Seattle

West Virginia

Johnson, Maurice E.....Pt. Pleasant
Livingstone, Robert C.....Clarksburg

Wisconsin

Doyle, Chauncey J.....Milwaukee
Elger, Harold E.....Waukesha
Hendrickson, Wm. O..Black River Falls
Kapke, Franklin W.....Milwaukee
Lieberman, Benjamin.....Milwaukee
Schmitz, Robert C.....Madison
Uszler, Louis B.....Milwaukee
Weller, Edgar A.....Weyauwega

Puerto Rico

Fiol, José.....Ponce
Rosario-Santos, Angel R.....Rio Piedras

RECALLED OR NOT RELIEVED FROM ACTIVE DUTY

Freeman, Joseph.....New London

MEDICAL OFFICERS RELEASED BY THE NAVY

NAVAL RESERVE MEDICAL OFFICERS RECOMMENDED FOR RELEASE FROM ACTIVE DUTY

Alabama

Burleson, Paul W.....Birmingham

Arizona

Barnes, Harry A.....Flagstaff
Jones, Robert E.....Phoenix

Arkansas

Crouse, John C.....Little Rock
Hearnsberger, Henry G.....Fordyce
Jackson, Haynes G.....Hot Springs
Mark, Philip F.....Eureka Springs

California

Abendroth, J. R.....Hayward
Briggs, Wilford M.....Las Jolla
Byron, Ralph L. Jr.....San Francisco
Chandler, Kennard T.....Oroville
Clock, Charles J.....Redlands
Coleman, Ralph L.....Oakland
Davis, Edward W.....Auburn
Davis, Stanley S.....Oakland
Egenolf, George F.....San Francisco
Ellis, Eugene J.....Beverly Hills
Farrier, Robert A.....Concord
Gallison, Frank E.....Los Angeles
Garbarino, Robert J.....Oakland
Goldkamp, Otto G.....San Diego
Hamlin, Edwin M.....Santa Rosa
Lamont, Herbert S. A.....Los Angeles
La Mont, Wynant.....Beverly Hills
McCoy, David A.....Los Angeles
McVann, Robert M.....Los Angeles
Modern, Frederick W. S.....Los Angeles
Ogara, Louis A.....San Francisco
Pederson, Earl S.....Oakland
Roberts, Walter L.....Los Angeles
Siefert, Herman J.....Los Altos
Smith, Seth W.....Laguna Beach
Stallone, Victor Jr.....Albany
Thomas, Sydney F.....Menlo Park
Viecelli, James D.....San Francisco
Welch, Richard E.....Long Beach

Colorado

Fralick, Ernest H.....Denver
Hipps, Chauncey J.....Denver
Morrell, Robert M.....Sterling
Penix, Lex L.....Denver

Connecticut

Brewer, Timothy F.....West Hartford
Darr, George C.....Middletown
Hepburn, Robert H.....West Hartford
Hopper, Edward B.....Glenbrook, Darien
Kimbell, Isham Jr.....New Haven
Murray, John G.....New Haven
Perkins, Woodbury.....Greenwich

Delaware

Johnson, Edgar N.....Wilmington

District of Columbia

Bailey, Joseph A.....Washington
Manion, William C.....Washington
Miller, Henry R.....Washington

Florida

Cannon, Edward M.....Coral Gables
Crumpler, Warren H.....Tampa
Linn, Frank D.....Warrington
Pearce, John L.....St. Petersburg
Taylor, Joseph W. Jr.....Tampa

Georgia

Atwater, John S.....Savannah
Bell, Arlis G.....Swainsboro
Duncan, George W.....Jeff Davis County
Farmer, Charles W. Jr.....Newnan
Gilbert, Benjamin P.....Atlanta
Gordon, Samuel I.....Atlanta
Sumner, Wilbur C.....Denton

Idaho

Henry, George W.....Blackfoot

Illinois

Aaberg, Edgar L.....Peoria
Ansprenger, Aloys G.....Galesburg
Blodgett, Pliny R.....Chicago Heights
Cutter, Robert L.....Evanston
Frost, Jack K.....Centralia
Galante, Vincent J.....Chicago
Gamm, Stanford R.....Chicago
Kane, Wendell L.....Herrin
Lee, Bruce D.....River Forest
McNeilly, Gordon C.....Utica
Moss, Charles T. Jr.....Urbana
Munro, John V. Jr.....Peoria
Naquin, Howard A.....Chicago
Shaw, Noel G.....Evanston
Sholder, Seymour.....Chicago
Sloan, Willard K.....Oblong
Stokoe, Robert S.....Chicago
Wendel, George I.....Chicago

Indiana

Crawford, James H.....Evansville
Findley, John W. Jr.....Crawfordsville
Fischer, Warren E.....Indianapolis
Millikan, Martin K.....Indianapolis
Phares, Robert W.....Greentown

Iowa

Burke, Edmund T.....Waterloo
Ferguson, John W.....Newton
Johnson, Richard M.....Manning
Kirch, Walter A.....Des Moines

Kansas

Anderson, William F.....Chanute
Carreau, Ernest P.....Wichita
Drake, Roy F.....Iola
Hall, Bernard H.....Laurence
Harrison, Lyman L. Jr.....Marysville
Kipp, Dean C.....Manhattan
Madtson, Alfred R.....Ottawa

Kentucky

Armstrong, Charles J.....Louisville
Darnell, Matthew C. Jr.....Frankfort
Petway, Willard J.....Louisville

Louisiana

Bain, William L.....New Orleans
Bender, Nathan J.....Shreveport
Bradburn, William P. III.....New Orleans
Gregoratti, Joseph V.....Gretna
Leon, William.....New Orleans
Torre, Mottram P.....New Orleans
Van Gelder, David W.....Baton Rouge

Maine

Giddings, Paul D.....Augusta
Roy, Robert L.....Lewiston
Temple, George L.....Lewiston

Maryland

Bieren, Roland E.....Baltimore
Cohn, Robert.....Bethesda
Mazer, Robert.....Baltimore
Nelson, Alfred T.....Baltimore

Massachusetts

Baldwin, Joseph V.....North Wilbraham
Bentley, John C. Jr.....Weymouth
Binder, Eugene N.....Chestnut Hill
Black, Melvin B.....Brighton
Bourne, George C.....Scituate
Brenner, Jacob.....North Easton
Byrne, Francis A. Jr.....Brookline
Carrigan, Walter E.....Ayer
Cashin, John C.....Adams
Chretien, Thomas E.....Somerville
Davidson, Samuel H.....Brookline

Massachusetts—Continued

Fahey, Robert J.....Winchester
Farrand, Robert E.....Lynn
Fiumara, Nicholas J.....Pittsfield
Foye, Lucian C.....Arlington
Graham, James H.....Melrose
Hill, John M.....Dorchester
Koenig, Arthur T. Jr.....Roslindale
McArdle, John J. Jr.....Lawrence
McCarthy, Francis D.....Chelsea
MacGregor, Charles A.....Brookline
Murphy, John C.....Pittsfield
Nesbit, Clayton W.....Pittsfield
Ohler, Robert L.....Newton Highlands
Sacco, John J.....Belmont
Schwartz, Isaac H.....Somerville
Seagrave, Kenneth H.....Paxton
Willard, Raymond D. Jr.....Charlton

Michigan

Coulter, William J.....Grosse Pointe
Cummings, Robert H.....Ann Arbor
Lobe, Sidney M.....Detroit
Love, James M.....Detroit
McKnight, Robert E.....Detroit
Tazelaar, Myron A.....Detroit
Tompsett, Arthur J.....Albion

Minnesota

Ahrends, Curtis F.....Minneapolis
Barber, Tracy E.....Crookston
Busse, Edwin A.....Minneapolis
Flynn, Bernard F.....Hibbing
Gillin, Lloyd I.....Murdock
Gilson, John S.....Minneapolis
Guenther, Theodore A.....Rochester
Jessivo, Charles M.....Duluth
Klein, William A.....St. Peter
Robertson, James S.....Austin
Schulberg, Verne A.....Minneapolis
Simon, Daniel S.....Virginia

Mississippi

Booth, James L.....Jackson
Feibelman, Nathan D. Jr.....Vicksburg
Fuller, James L.....West Point
Kimbriel, Albert C. Jr.....Drew
McLarty, Chester A.....Oxford
Rich, Charles A.....Gulfport
Sautter, William A.....Jackson
Wiener, Julian.....Canton

Missouri

Bassett, Philip H.....St. Louis
Blankenship, George W.....Southwest City
Gilliland, Oliver M.....Kansas City
Haight, John M.....Kansas City
Hume, David M.....St. Louis
Lytton, William B.....Clayton
Miller, Winston R.....Independence
Platt, Paul C.....Kansas City
Shears, Robert N.....Kansas City
Trueblood, Alva C. Jr.....Webster Groves
Weiford, Edward C.....Kansas City

Montana

Spratt, Robert J.....Butte

Nebraska

Adams, Wendall W.....Grant
Albertson, Leland C.....Kearney
Heller, Philip H.....Lincoln
Hilsabeck, John R.....Gretna
Jackman, Herbert S.....Omaha
Mitchell, Howard E.....South Sioux City
Paris, Arthur S.....Omaha

Nevada

Lewis, Charles J.....Carson City

New Hampshire

Shaw, Paul S.....Bristol

V 132
1946

MEDICAL OFFICERS RELEASED BY THE NAVY

New Jersey

Baganz, Crawford N.....Lyons
Cameron, Charles S. Jr.....Rutherford
Dwyer, Gregory K.....Essex Falls
Forrest, Arnold W.....South Orange
Fruchtbaum, Robert P.....Nutley
Gilbert, George G.....Madison
Gray, Samuel H.....Kirkwood
Hile, Harry E. Jr.....Collingwood
Holder, Lester.....Newark
Kerdasha, Richard.....North Bergen
Lieberson, Leonard.....West New York
Lockward, Howard J.....Caldwell
Shoukimas, John.....Cranford
Staub, Robert J.....Millburn
Thompson, Charles M.....Haddonfield
Zampella, Arthur D. L.....Jersey City

New Mexico

Reymont, Anthony E.....Santa Fe

New York

Akelaitis, Andrew J. E.....Rochester
Anderson, Harold T.....Jamestown
Coleman, Frederick W. Jr..Baldwin, L. I.
Comer, John V.....Brooklyn
Denton, George R.....Albany
Dotter, Charles T.....Freeport
Fioretti, Ralph J.....Tuxedo
Fisher, Allan A.....Rochester
Floersheim, Milton Jr.....Buffalo
Freed, Leonard.....Brooklyn
Gonzalez, Frederick J.....New York
Harris, Joseph H.....New York
Hartson, Robert C.....Syracuse
Jackson, William M.....Rochester
Klopp, Calvin T.....Long Island City
Kohl, Mathias F. F.....Rochester
Linden, Arthur C.....Peekskill
Lombard, Joseph.....Brooklyn
McAteer, James.....New York
Osmundsen, Robert N.....Hempstead
Osborne, Frank G. Jr.....Brooklyn
Pearson, Claude W.....New York
Redish, Milton H.....New York
Rowe, Arthur T.....Mt. Vernon
Runfola, Anthony V.....Cortland
Ryan, Edward S.....New York
Saeli, Amadeo B.....Savannah
Smolen, Elwyn M.....Bronx
Spector, Samuel.....Brooklyn
Spindler, Howard A.....Rochester
Stoller, Elias.....Bronx
Williams, H. J...Jackson Heights., L. I.

North Carolina

Dorenbusch, Alfred A.....Charlotte
Hadley, Herbert W.....Greenville
Sain, Fletcher D.....Littleton

North Dakota

Dyrud, Jarl E.....Maddock

Ohio

Auringer, Arthur J.....East Cleveland
Brill, Thomas M.....Youngstown
Burkhart, Samuel E.....East Cleveland
Clouse, Michael Paul Jr.....Somerset
Courter, Sanford R.....Cincinnati
D'Orazio, Edward.....Steubenville
Dumais, Aloid F.....Lakewood
Eddy, Ford E.....Marietta
Grover, William L.....Columbus
Harding, Warren G. II.....Columbus
Harrison, DeWitt E.....Alliance
James, David W.....Youngstown
Kamellin, Eli.....Cleveland
Knight, Frederick H.....Grafton
Luros, John T.....Toledo
McCaffrey, Eugene J.....Cleveland
Posey, Frank M. Jr.....Cleveland
Roukema, Frederick J. T.....Greeley
Ryan, Joseph M.....Columbus
Scheib, Burton V. D.....Toledo
Schumacher, Paul C.....Hamilton

Oklahoma

Aycock, Bryon W.....Lawton
First, Francis R. Jr.....Chicotah
McIntyre, John A.....Tryon
Parsons, Orval L.....Lawton
Tefertiller, Charles L.....Arnett

Oregon

Anderson, Orville J.....Portland
Lockwood, Milton C.....Portland
Loggan, Powell B.....Burns
Schluter, Harold G.....Pendleton
Swett, William J.....Portland

Pennsylvania

Allen, John D.....Moylan
Balsbaugh, Edward F.....Annville
Bortz, Donald W.....Greensburg
Burleson, Norres M.....Port Allegany
Byrne, John J.....Philadelphia
Campbell, James C.....Pittsburgh
Dattilo, James T.....Pittsburgh
Elder, Eldon G.....Pittsburgh
Evans, Thomas M.....Bridgeville
Ferraro, William A.....Pittsburgh
Gutch, Charley F.....Upper Darby
Hamilton, William A.....Philadelphia
Healy, Timothy P.....Altoona
Kinsell, Laurance W.....E. Stroudsburg
Klem, Albert J.....Forty-Fort
Leute, William R. Jr.....Upper Darby
Levit, Samuel.....Philadelphia
McCarron, Daniel J.....Philadelphia
Miller, Joseph A.....Pitcairn
Modisher, Melvin W.....Meadville
Rauer, Lester.....Philadelphia
Regan, Cornelius J.....Drexel Hill
Robertson, Alexander R. IV.....Ardmore
Sangston, Russell E.....Uniontown
Schaffner, John P. Jr.....Philadelphia
Sinkler, Wharton Jr.....Chestnut Hills
Smith, Edward A. Jr.....Philadelphia
Statti, Louis W.....Pittsburgh
Stauffer, Howard H.....Hershey
Wilson, William M. Jr.....Philadelphia
Wheelock, Mark C.....Pittsburgh

Rhode Island

Halbach, Robert M.....Jamestown
Roque, John A.....Edgewood

South Carolina

All, Frank E.....Allendale
Davis, Harry A. Jr.....Sumter
Edenfield, Jess R. Jr.....North Augusta
Edgerton, Norman B.....Orangeburg
Furman, Irvine K. Jr.....Charleston
Jowers, Lawrence V.....Columbia
McKey, John D.....Spartanburg
Martyn, Wilford E.....Aberdeen
Quinn, Robert H.....Yankton

Tennessee

Brown, James S. Jr.....Kingsport
Hinton, James K. Jr.....Collierville
Ryan, Eugene M.....Springfield

Texas

Anderson, Roland B.....Dallas
Bagwell, Robert W.....Austin
Baldwin, Russell E. G.....Memphis
Bellegie, Nicholas J.....Galveston
Benson, Billy F.....Fort Worth
Blanco, Victor M.....San Antonio
Brown, Arnold L.....Dalhart
Bryan, John N.....Houston
Callaway, Sam E.....El Paso
Clifford, William S.....Austin
Ellis, Frank A.....Corpus Christi
Gready, Thomas G. Jr.....Galveston
Herndon, Ray F.....Houston
Hilliard, George H. Jr.....Canton
Kaminsky, Dave.....Houston
Lillie, Gordon V.....Sherman
Lipcon, Harry H.....Fort Worth

Texas—Continued

Pruet, Royce W.....Eastland
Richards, Fred V.....Tulia
Rix, Robert A. Jr.....Commerce
Sawtelle, William W.....San Antonio
Scott, John H.....Houston
Scull, Thomas J.....San Antonio
Thomason, Robert H.....Huntsville
Winn, Robert E.....Dallas
Withers, Henry W.....Houston
White, Roland L.....Galveston

Utah

Ballard, Ross L.....Draper
Judd, Thomas R.....LaVerkin
Larsen, Boyd J.....Lehi

Vermont

Hadley, Richard B.....Burlington
White, Philip F.....Craftsbury Common

Virginia

Bagby, Richard A.....Edwardsville
Barksdale, Edwin E.....Danville
Fry, Wesley.....Alexandria
Gasque, McRoy Jr.....Charlottesville
Hill, John H.....Charlottesville
Holcomb, Frederic W. Jr..Charlottesville
Kirschman, Robert E.....Newport News
Orr, Alva D.....Glade Spring
Psimas, Constantine N.....Norfolk
Radl, Cyril J.....Arlington
Ward, Charles H.....Warsaw
Wolfe, Harold E.....Marion

Washington

Allen, Clifford V.....Longview
Armstrong, William F.....Vancouver
Callahan, John J.....Wapato
Callison, Robert D.....Seattle
Huber, Dale G. Jr.....Edmonds
Lagozzino, Donato A.....Seattle
Rykken, Felix C.....Bellingham
Schneider, Alvin J.....Seattle
Williams, Paul L.....Bellingham

West Virginia

Allebach, Newton W.....Charleston
Batten, James C.....Parkersburg
Bush, John A. K.....Warrington
Clapham, Roger E.....Martinsburg
Corbitt, Richard W.....Parkersburg
Dillinger, Karl A.....Weston
Hedrick, Thomas A.....Beckley
Jarvis, Shiras M.....Clarksburg
Klyza, Stanley J.....Clarksburg
Kroll, Peter G.....Welch
Rueckl, Frank V. Jr.....Weston
Sawyers, Thomas M.....Hinton
Schall, Roy F.....Charleston
Smith, Wilson P.....Huntington
Staker, Norman W.....Kermit
Warman, Milton M.....Morgantown
Weller, Eli J.....Hollidays Cove

Wisconsin

Boyce, David C.....Wauwatosa
Detjen, Edward D.....Algoma
Flaherty, Gervase S.....South Milwaukee
Grabiec, Max V.....Portage
Grinney, Leo R.....Racine
Gruender, Jack M.....Milwaukee
Keck, Carleton A.....Milwaukee
Kuritz, Albert B.....Milwaukee
Schilling, Robert F.....Adell
Stutzman, Jacob W.....Madison
Temple, John W.....Fond du Lac

Wyoming

Hart, Wilber.....Midwest

Hawaii

Hill, Rogers L.....Kauai
McCorriston, Collin C.....Honolulu
Strathairn, Thomas S.....Honolulu

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

CALIFORNIA

Grant for Research.—A cancer research project at the Queen of Angeles Hospital, Los Angeles, will be financed by a grant of $5,000 from the Lillian Josephs Foundation. The work is being carried on by Drs. Lowell S. Goin and Eugene F. Hoffman, who for the past six years have been interested in contact x-radiation therapy, administered through a suprapubic cystotomy, for certain types of bladder carcinoma. According to the *Bulletin* of the Los Angeles County Medical Association, a small series of cases has been treated and the results (including some five and six year cures) have been very encouraging. The procedure requires about three weeks hospitalization and it is to assist this hospitalization cost that the Josephs foundation has made the grant. To benefit under the program the patient must be financially unable to bear the involved expense, the carcinoma must be proved by biopsy, must involve some portion of the trigone, must not exceed 3 cm. in diameter and no metastases can be present.

DISTRICT OF COLUMBIA

Appointments at George Washington University.—Among the new appointments to the faculty of the George Washington University School of Medicine are the following:

Dr. Brian B. Blades, professor of surgery and executive officer of the department of surgery.
Paul K. Smith, Ph.D., professor of pharmacology and executive officer of the department.
Dr. Lloyd H. Mousel, clinical professor of anesthesiology.
Dr. Vincent M. Iovine, adjunct clinical professor of surgery.
Dr. Monroe J. Romansky, associate clinical professor of medicine.
Dr. Wallace H. Graham, professorial lecturer in surgery.
Dr. Clark H. Yeager, professorial lecturer on tropical medicine.
Dr. Webb E. Haymaker, professorial lecturer in anatomy.
Carleton R. Treadwell, Ph.D., assistant professor of biochemistry.
Dr. William S. McCune, assistant clinical professor of surgery.

FLORIDA

Industrial and Railway Surgeons Merge.—With the consolidation of the Florida Association of Industrial Surgeons and the Florida Association of Railway Surgeons, the Florida Association of Industrial and Railway Surgeons has been formed. Dr. Ferdinand A. Vogt, Miami, is president; Dr. Lloyd J. Netto, West Palm Beach, president-elect; Dr. Edward W. Cullipher, Miami, vice president, and Dr. John H. Mitchell, Jacksonville, secretary-treasurer.

ILLINOIS

Chicago

Personal.—Edson Lichty, who has served as assistant director in charge of enrolment of the Blue Cross Plan for Hospital Care in Chicago since September 1944, has just been elected executive director of that plan.

Dr. Volini Named to School Board.—Dr. Italo F. Volini, professor and head of the department of medicine, Loyola University School of Medicine, has been named a member of the school board of the city of Chicago. The appointment was by Mayor Edward J. Kelly.

The Belfield Memorial Lecture.—Dr. Hugh J. Jewett, assistant professor of urology, Johns Hopkins University School of Medicine, Baltimore, will deliver the annual William T. Belfield Memorial Lecture before the Chicago Urological Society, October 24, on "Bladder Tumors."

The First Pusey Lecture.—The Institute of Medicine of Chicago will present the first William Allen Pusey Lecture on October 25 at a meeting with the Chicago Dermatological Society and the Chicago Society of Internal Medicine. Dr. Udo J. Wile, Ann Arbor, will speak on "Some Obscure and Paradoxical Problems of Syphilis." Dr. Pusey, who was a Past President of the American Medical Association, died Aug. 29, 1940.

Appointments at Illinois.—Dr. Roger A. Harvey, Rochester, N. Y., has been appointed professor and head of the department of radiology at the University of Illinois College of Medicine and Dr. David Shakow, New York, professor of psychiatry. The University of Illinois has acquired the properties of the former Mayo General Hospital, Galesburg, for use as classrooms and for student housing. The permit will be in force until a three year lease is approved by the War Assets Administration. The former hospital facilities, comprising ninety one-story buildings, will house 2,000 students. They will be ready for occupancy on October 15.

Dr. Ivy Resigns from Citizens' Group.—Dr. Andrew C. Ivy, vice president of the Chicago Professional Colleges, University of Illinois, announced his resignation, September 24, from the Midwest Science and Technology Division of the Independent Citizens Committee of Arts, Sciences and Professions. He was a member of the executive committee of the science division. Dr. Ivy is reported to have said that the committee made moves which were "decidedly contrary" to his views and that he objected particularly to the committee's support of "compulsory health insurance." Instead he favors a sliding scale based on income to subsidize expensive medical care items.

INDIANA

District Meeting.—The Eleventh Indiana Councilor District Medical Association met at Marion September 18. The following spoke:

Dr. Donald R. Adams, Indianapolis, Outpatient Services to Veterans.
Dr. Stewart T. Ginsberg, Marion, Mental Hygiene.
Dr. David A. Boyd Jr., Marion, Psychosomatic Medicine.
Ross F. Lockridge, Litt.D., Bloomington, subject not announced.

Personal.—Mrs. Winifred Kahmann, Indianapolis, director of occupational and physical therapy at the Indiana University Medical Center, has been elected president of the American Occupational Therapy Association.——Dr. Thomas Dobbins, medical director of Servel, Inc., Evansville, and for many years in charge of medical and safety matters for that company, resigned July 12 because of ill health. His work has been taken over temporarily by Dr. William L. Daves, Evansville, recently released from military service.

Certification of Causes of Death.—According to a new state law the coroner, who heretofore has certified the cause of deaths, has been relieved of this duty and it becomes the duty of the physician last in attendance, according to the Jeffersonville *Post*, August 29. The new law of the Indiana Acts of 1945, passed on by James A. Emmert, attorney general of Indiana, in Official Opinion No. 55, went into effect September 1. The attending physician is required to use a form prepared by a funeral director, and if the cause of death was without medical attendance or the physician last in attendance fails to sign certificate of death, it becomes incumbent on the local health officer to investigate and certify to the cause of death on the basis of information obtained from persons having knowledge of the facts. In no case does the coroner certify to the cause of death. The funeral director does not sign the certificate of death, and the cause of death should be certified only by the attending physician or the local health officer under the facts of the particular case. In the event of death by violence or casualty, the coroner views the body and holds an inquest. He is required to file the verdict with the clerk of the circuit court of the county in which the body is found.

"Diabetic Institute" Investigated.—The Indianapolis Better Business Bureau is said to have charged September 10 that a "diabetic institute" offered a "quick cure" which had resulted in the death of "many persons," newspapers reported. The bureau filed a petition for revocation of the medical license of Dr. Charles Kaadt, Fort Wayne, with the Indiana State Board of Medical Registration and Examination, charging that he was the operator of the Kaadt Diabetic Institute in South Whitley. The so-called exposé is said to stem from the articles of a reporter printed in the Muncie *Star*. The reporter, Robert E. Johnson, stated in his stories that he was treated at the Kaadt Diabetic Institute under the name of Robert Cook. Dr. Kaadt was believed to be "resting" in the South while his brother, Peter S. Kaadt, was continuing the operation of the institute, the Indianapolis *News* stated on September 11. The press reports indicated the "treatment" to be a "quick" three day "cure" with freedom from use of the customary insulin and dietary controls and the prescription to be a "secret formula" obtained "exclusively" at the institute. Reports of harmful effects resulting from the Kaadt treatment led bureau investigators to hold the institute under surveillance for more than a year. The Indianapolis Better Business Bureau is said to have filed its petition with the state board of registration in medicine on the results of the investigation.

V 132
1946

MICHIGAN

Le Moyne Snyder Joins Detective Agency.—Dr. Le Moyne Snyder, Lansing, legal medical director of the Michigan State Police, announced on September 6 his association with four prominent persons in the formation of a detective agency, Scientific Evidence, Washington, D. C. Associated with Dr. Snyder will be Ray Schindler, top ranking New York detective; Clark Sellers, nationally known handwriting expert; W. W. Harper, California physicist and scientist, and Leonarde Keeler, LL.D., Chicago, developer of the polygraph lie test. Dr. Snyder said, according to newspaper reports, that he will retain his position with the state police but will discontinue his private practice in Lansing. He graduated at Harvard Medical School, Boston, in 1923 and was admitted to the bar in 1934.

NEW YORK

Medical Lectures in Industrial Plants.—With a talk, September 5, on "Early Ambulation of Surgical Patients," Dr. Donald D. Kozoll, Evanston, Ill., launched a series of lectures sponsored by the medical department of the Corning Glass Works, Corning. Lectures in the series will be given semiannually and are indicative of the plan of modern industry to bring new advancements to physicians in different communities.

New York City

Motion Picture Theater Offers Accommodations for Invalids.—The Park Avenue Theater, a subscription motion picture house, which is to open some time in the latter part of October, will have special accommodations for those confined to wheel chairs, enabling invalids to see the show without leaving their wheel chairs. All seats are sold only on a subscription or reserved seat basis. An accurate seating chart of each show is kept in the manager's office. Whenever one of the audience is wanted on the telephone the call is referred to the manager's office and an usherette calls the person to the phone. There will be no standing in line. Should a patron be hard of hearing, special earphones will be provided for his use.

Institute of Tropical Medicine for Liberia.—In honor of the one hundredth anniversary of the independence of Liberia, Harvey F. Firestone Jr., president of the Firestone Tire & Rubber Company, has given $250,000 to establish an Institute for Research in Tropical Medicine as a memorial to his father, founder of the company. The company, which set out to produce rubber independent of the Far East, now has 75,000 acres of rubber trees in Liberia, according to the Chicago *Sun*. Dr. Thomas T. Mackie, president of the American Foundation for Tropical Medicine, which will operate the institute, accepted the gift at a dinner in the Waldorf Astoria, September 20. William V. S. Tubman, president of Liberia, sent a cablegram accepting the gift.

NORTH CAROLINA

Dr. Ferrell Named to Medical Care Commission.—Dr. John Ferrell, Stamford, Conn., recently associated with the John and Mary Markle Foundation, New York, has been appointed adviser and consultant executive secretary of the North Carolina Medical Care Commission. Dr. Clement C. Clay resigned as executive secretary, effective September 30.

OHIO

Fall Lectures.—On September 17 the Academy of Medicine of Cincinnati opened its fall program with talks by Drs. David A. Tucker Jr. and Charles E. Hauser, both of Cincinnati, president and president-elect respectively. Other lectures in the 1946-1947 series include:

Dr. Robert C. Rothenberg, Cincinnati and Thomas A. Hendricks, Chicago, October 1, The Medical Economics Picture Today—What Can We Do About It?
Dr. Elliott P. Joslin, Boston, October 15, Diabetes (joint meeting with the Diabetes Council).
Dr. Bayard T. Horton, Rochester, Minn., November 12, Headache—Diagnosis and Treatment.
Dr. Edward B. Tuohy, Rochester, Minn., November 26, Anesthesiology—Practical Considerations and Current Prospectus (joint meeting with the Cincinnati Society of Anesthesiology).
Dr. Franz G. Alexander, Chicago, December 3, The Psychosomatic Approach of the Disturbances of the Vegetative Functions.
Dr. Richard B. Capps, Chicago, December 17, Infectious Hepatitis.
Dr. Reginald H. Smithwick, Boston, January 7, The Surgical Treatment of Hypertension.
Dr. Edgar V. Allen, Rochester, Minn., January 21, The Present Status of Anticoagulant Therapy.

TEXAS

Randolph Clark New Director of Cancer Hospital.—Dr. Randolph L. Clark Jr., recently discharged lieutenant colonel in the Army Air Forces Medical Corps, has assumed his duties as the new director of the M. D. Anderson Hospital for Cancer Research, state hospital under the University of Texas. Dr. Ernest W. Bertner, Houston, who accepted the position of acting director of the hospital on a temporary basis at its inception in 1941, resigned to devote all his time to the duties of president of the Texas Medical Center, of which the Anderson Hospital is an important part. A resolution was adopted by the University of Texas Board of Regents commending Dr. Bertner for his service. Dr. Clark graduated at the Medical College of Virginia, Richmond, in 1932. After entering the A. A. F. Medical Corps in 1942 he organized the department of experimental surgery at the Aero Medical Laboratory at Wright Field and later was director of the department of surgery at Randolph Field, San Antonio.

Pediatric Conference.—The fourth postgraduate conference in pediatrics will be held in Galveston, October 28-November 2, under the direction of the University of Texas Child Health Program and the division of maternal and child health of the Texas State Health Department. The program, which will include round tables, symposiums and clinics, will cover the problem of diarrhea in infants, endocrine disorders in children, splenomegaly as a diagnostic problem, acute contagious diseases of childhood, neurologic problems in childhood, encephalitis and abdominal pain in children. The guest speakers are:

Dr. Myron Wegman, professor and chairman, department of pediatrics, Louisiana State University School of Medicine, New Orleans.
Dr. Wilburt C. Davison, professor and chairman, department of pediatrics and dean, Duke University School of Medicine, Durham, N. C.
Dr. Franklin H. Top, associate professor of preventive medicine and public health, Wayne University College of Medicine, Detroit.
Dr. Douglas N. Buchanan, associate professor of pediatrics, University of Chicago School of Medicine.
Dr. Julian D. Boyd, professor of pediatrics, State University of Iowa College of Medicine, Iowa City.
Dr. Daniel C. Darrow, associate professor of pediatrics, Yale University School of Medicine, New Haven.
Russell K. Smith, D.D.S., assistant professor of preventive medicine, University of Texas School of Dentistry.

VIRGINIA

Changes in Health Personnel.—Dr. Fred Wampler, Richmond, has been named director of the Page-Warren-Shenandoah Health District, Virginia State Department of Health, effective September 1.

Automobile Presented to Physician.—Dr. Oscar L. Ramsey, who has practiced in Gretna for forty years, was presented with an automobile June 1, the gift of the community. The plan to honor the physician was sponsored by the Gretna chamber of commerce.

State Medical Meeting.—The ninety-eighth meeting of the Medical Society of Virginia will be held at the Cavalier Hotel, Virginia Beach, October 14-16, under the presidency of Dr. Julian L. Rawls, Norfolk. Among the speakers will be:

Dr. Millard B. Savage, Norfolk, Occiput Posterior and Its Treatment.
Dr. George A. Wright, Marion, Complicated Surgery of the Abdomen, with Special Reference to Anesthesia, Drainage, Preoperative and Postoperative Care, with Case Reports.
Dr. Frank S. Johns, Richmond, Carcinoma of the Colon.
Dr. A. Stephens Graham, Richmond, Current Trends in Surgery of the Colon and Rectum for Cancer.
Dr. Harry J. Warthen Jr., Richmond, The Need in Virginia for Trained Medical Physician Anesthetists.
Dr. Charles H. Lupton, Norfolk, The Treatment of Burns.
Dr. Russell V. Buxton, Newport News, Unusual Tumors of the Abdomen.
Dr. Everett I. Evans, Richmond, Surgical Treatment of Hypertension and Peripheral Vascular Disease.
Dr. Frank P. Coleman, Richmond, Primary Carcinoma of the Lung.
Dr. Edwin E. Barksdale, Washington, D. C., Penicillin in Syphilis.
Drs. George A. Welchons and Edwin L. Kendig Jr., Richmond, Lung Abscess in Infants and Children: Treatment with Penicillin.
Dr. John F. Williams, Richmond, Practice of Psychosomatic Medicine.
Drs. Charles M. Caravati and James M. MacMillan, Richmond, Gastroscopy: An Aid in the Diagnosis of Occult Hematemesis.
Drs. Morton M. Pinckney, James O. Burke, William Taliaferro Thompson Jr. and Henry S. Tucker, Richmond, Infectious Hepatitis.
Drs. John L. Guerrant and Oscar Swineford Jr., Charlottesville, The Cocaasonal Treatment of Hay Fever.
Drs. Robert F. Gayle Jr. and Claude L. Neale, Richmond, Present Status of Shock Therapy.
Dr. James L. Thomason, Norfolk, The Diagnosis and Treatment of Herniated Nucleus Pulposus.
Drs. Paul D. Camp and Louise F. Galvin, Richmond, Severe and Fatal Rheumatic Fever with Pancarditis in Virginia.

One session will be devoted to a symposium on general practice. Dinner meetings will be addressed by Dr. George F. Lull, Secretary and General Manager, American Medical Association, and Dr. Joseph S. Lawrence, director, Washington office, Council on Medical Service of the Association.

GENERAL

Accident Facts.—The National Safety Council has recently released its 1946 edition of Accident Facts. The first issue was published in 1921. The booklet contains statistical information on the number and type of accidents occurring throughout the country. The National Safety Council has offices at 20 North Wacker Drive, Chicago 6.

Lucius Johnson Joins College of Surgeons.—Rear Admiral Lucius W. Johnson (MC), retired, Washington, D. C., is now affiliated with the American College of Surgeons, serving as field representative in the Pacific Coast area, where he is conducting hospital standardization and graduate training in surgery surveys. Dr. Johnson, who received a D.D.S. at the University of Pennsylvania School of Medicine, Philadelphia, in 1903 and an M.D. in 1907, entered the navy in 1908.

Expedition to Collect Monkeys.—A six month expedition into the jungles of the Netherlands East Indies and Philippine Islands has been planned by the National Foundation for Infantile Paralysis to establish methods for collecting, housing, transporting and protecting from contamination monkeys vitally needed to continue research on poliomyelitis. Mr. John N. Hamlet of the U. S. Fish and Wildlife Service has been obtained on a leave of absence basis to make the trip. He has had considerable experience in this field, including an expedition into southern Mexico, Yucatan and British Honduras to collect poisonous reptiles. He and Harry M. Weaver, Ph.D., acting director of research for the National Foundation, at a press conference September 16 at the Hotel Willard, Washington, D. C., explained the details of the expedition and the need for the monkeys in research laboratories as well as the assistance given to the project by the State, War, Navy and Interior departments as well as the British, Dutch and Philippine governments.

Association of Military Surgeons.—The Association of Military Surgeons will hold its annual meeting in Detroit, October 9-11. Scientific general meetings will be held each day bringing out the latest in medical knowledge as developed during the war, particularly as to how this military knowledge is applicable to civilian practice. In addition there will be section meetings of the various specialties and the coordination services of the medical corps such as dental, sanitary, nursing and veterinary corps. The banquet will be held on the evening of October 9; present will be Surg. Gen. Norman T. Kirk of the Army, Surg. Gen. Ross McIntire of the Navy, Surg. Gen. Thomas Parran of the U. S. Public Health Service, Gen. Paul R. Hawley, medical director of the Veterans Administration, and General Smith of the dental corps of the army. Present at the meeting will be the Surgeon Generals of Great Britain, the Netherlands, the East Indies, Spain, Belgium, Poland, Sweden, Denmark, Nicaragua, Australia, New Zealand, British South Africa and Canada and probably others. Scientific exhibits will be shown by the army and navy among others, and a large commercial exhibit is expected. Percy Jones Hospital will have an interesting exhibit.

Dr. Walmer Named Medical Director of Industrial Foundation.—Dr. Charles R. Walmer, Pittsburgh, has been appointed medical director of the Industrial Hygiene Foundation of America, 4400 Fifth Avenue, Pittsburgh 13. Dr. Walmer will hold the rank of senior fellow in the Mellon Institute, of which the foundation is a part. As a full time physician for Industrial Hygiene Foundation, Dr. Walmer will direct the medical phases of the foundation's work for the improvement of working conditions and the advancement of employee health in industry. He will also serve as secretary of the foundation's medical committee, which is headed by Dr. Anthony J. Lanza, associate medical director, Metropolitan Life Insurance Company, New York. For the past five years Dr. Walmer has been associated with Dr. Theodore L. Hazlett, Pittsburgh, medical director at Westinghouse Electric Corporation, serving as toxicologist and as a consulting specialist in industrial medicine. Dr. Walmer graduated at the University of Pittsburgh School of Medicine in 1938.

Heart Fellowships Awarded.—Two fellowships have been awarded by the American Legion and its auxiliary through the American Heart Association. The recipients are the New York University College of Medicine and the House of the Good Samaritan, Boston. In New York the fellowship will be used for the support of Dr. Samuel T. Schlamowitz, New York, who will act as research fellow under Dr. Arthur C. De Graff, New York, and Dr. Samuel A. Brown, professor of therapeutics, New York. Dr. Schlamowitz, a veteran, will perform a biochemical study of patients suffering from rheumatic fever, with particular reference to the chemistry of the body as it relates to rheumatic fever. In Massachusetts Dr. Joseph E. Warren, Boston, will study under the direction of Dr. T. Duckett Jones, Boston, and will be concerned with the changing glandular conditions of the body affecting rheumatic conditions. Dr. Warren participated in the airborne invasions of Normandy and the Netherlands and in the defense of Bastogne. The legion and its auxiliary gave $50,000 May 11 to the American Heart Association (THE JOURNAL, June 15, p. 620). The fellowships are being handled through the American Council on Rheumatic Fever of the American Heart Association (THE JOURNAL, June 22, p. 696). Each of the fellowships is available for a period of three years and carries a stipend of $3,500, $4,000 and $5,000 for the first, second and third years respectively.

International Hematology and Rh Conference.—An International Hematology and Rh Conference will be held in Dallas, Texas, November 15, in affiliation with the second Mexican Blood Transfusion Congress in Mexico City, November 17-25. The morning session will be held at the Adolphus Hotel. Dr. Joseph M. Hill, director of the William Buchanan Blood, Plasma and Serum Center, Baylor University Hospital, Houston, will preside. The afternoon session will be held at the Medical Library of Baylor University Hospital. Dr. Eduardo Uribe Guerola, president of the second Mexican Blood Transfusion Congress, will preside. The guest speakers are:

Dr. Philip Levine, Linden, N. J.
Dr. Robert R. Race, Lister Institute of Preventive Medicine, London, England.
Dr. William Dameshek, Boston.
Dr. Ernest Witebsky, Buffalo.
Dr. Israel Davidsohn, Chicago.
Dr. Ludwig Hirszfeld, University of Wroclaw, Wroclaw, Poland.
Dr. Ignacio Gonzalez Guzman, University of Mexico College of Medicine, Mexico City.
Dr. Guerola.
Dr. Hill.

Reservations should be made with Sol Haberman, Ph.D., William Buchanan Blood, Plasma and Serum Center, Baylor University Hospital, Dallas, before November 5.

Visitors to the United States.—The British Commonwealth Scientific Office announces the following visitors to the United States, among others: Dr. F. C. MacIntosh of the staff of the Medical Research Council spent a week or ten days during the latter part of August visiting American and Canadian laboratories. Dr. D. W. Henderson of the Ministry of Supply is now in the United States for a stay of about two months; Dr. Henderson, who is the chief superintendent of the microbiologic department at Porton, is attached to the office of Mr. Kingan, British chemical warfare representative. Dr. S. R. Elsden, a member of the unit of animal physiology of the Agricultural Research Council, will arrive in the United States in September for one year at the invitation of Cornelius B. Van Niel, D.Sc., of the California Institute of Technology and Horace A. Barker, Ph.D., University of California, Berkeley, to work in their respective laboratories and to study, *inter alia*, American technics in the field of microbiology. Drs. Jethro Gough and J. B. Duguit are spending several weeks in the United States investigating the aluminum treatment of silicosis. Both are members of the department of pathology of the Welsh National School of Medicine, Cardiff. The visit is being made on behalf of the Pottery Manufacturers of Great Britain and is sponsored by the Ministry of Health. Information concerning these visitors may be obtained from Mrs. V. Connell, technical assistant to Dr. A. King, director of the United Kingdom Scientific Mission, British Commonwealth Scientific Office, Room 505, 1785 Massachusetts Avenue N.W., Washington, D. C.

Training Program of Cancer Institute.—The training program of the National Cancer Institute, designed to increase the ranks of medical specialists in the diagnosis and treatment of cancer, has been accelerated through funds recently appropriated by Congress resulting in fifteen new appointments, the U. S. Public Health Service announced August 20. The training program is considered to be one of the most effective means of making better diagnostic treatment and services available for cancer patients. Although the program was begun a few months after the institute was established in August 1937, it was curtailed during the war. Up to July 1, eighty-two physicians had received the specialized training provided by the traineeships awarded by the institute. At that time seven physicians were still in training, twenty-three new trainees

V 132
1946

went on duty during July, and the fifteen recommended for August will raise the total to forty-five. With its program currently expanding, it is expected that the total will be greatly increased by the end of the year. The physicians spend from one to three years in training at a cancer hospital or in a hospital with a large cancer service. The new appointees and the training centers where they will study are:

Drs. Milton Robbins, Maurice A. Weisberg, Max W. Mattes and Leonard S. Ellenbogen, at Bellevue Hospital, New York.

Drs. William G. Cahan, Neil P. Beall Jr., Warner L. Guiss, Arthur James, Allen H. Minor, George H. Parks, Theodore O. Winship and Oliver Moore, all at the Memorial Hospital for the Treatment of Cancer and Allied Diseases, New York.

Drs. Harry W. Mixer and Arnold J. Kremen at the University of Minnesota Hospital, Minneapolis.

Dr. Oscar H. Whiting at Freedmen's Hospital, Washington, D. C.

Praise Medical Mission to Czechoslovakia.—Wireless reports received by the American press September 23 indicate that a medical mission sent to Czechoslovakia has been publicly praised and credited with rendering "a lasting and inestimable service" during its two months' stay there. The mission constituted what was actually a "faculty on wheels" which journeyed from one end of the country to the other. Never before had a similar mission made so thorough and so complete a medical survey of a nation, it was stated. The staff visited hospitals, treated patients, performed operations, conducted 150 clinical conferences and delivered 230 lectures. Dr. Alexander Brunschwig, University of Chicago School of Medicine, performed a pneumonotomy, with Dr. Emery A. Rovenstine, New York, University College of Medicine, administering anesthesia, the first of its kind performed in Czechoslovakia, it was said. Other physicians in the mission include:

Dr. Paul D. White, Boston, Harvard University, chairman.
Dr. Erwin Kohn, New York, administrative officer.
Dr. Leo M. Davidoff, Columbia University College of Physicians and Surgeons, New York.
Dr. Ralph W. Gerard, University of Chicago College of Medicine.
Dr. L. Emmett Holt Jr., New York University College of Medicine.
Dr. Otto Krayer, Harvard.
Milan A. Logan, Ph.D., University of Cincinnati College of Medicine.
Dr. Everett D. Plass, State University of Iowa College of Medicine, Iowa City.
Dr. James E. Thomson, Lincoln, Neb.
Dr. Joseph F. Volker, Boston, Tufts College Medical School.

The University of Prague has awarded all the members of the mission its own medal, given to those who render it special or distinguished service, and the Czech cabinet is conferring the group with its highest honor, the Order of the White Lion. UNRRA is setting aside a sum of money to purchase necessary equipment to enable medical schools and the medical profession in Czechoslovakia to perpetuate and universalize the lessons learned from the American medical mission.

Work of Commission on Hospital Care Continued.—The American Hospital Association, Chicago, has announced the establishment of a department within the association for the purpose of continuing certain of the functions initiated by the Commission on Hospital Care after the commission disbands on October 1. In cooperation with the U. S. Public Health Service the association will continue to code and tabulate hospital schedules for state survey commissions through the Chicago office of the American Hospital Association. The work will be done in accordance with methods acceptable to the U. S. Public Health Service, utilizing public health service personnel and tabulating equipment located in the Chicago district office. Application to the W. K. Kellogg Foundation and the National Foundation for Infantile Paralysis for grants of $10,000 a year for two years from each foundation was authorized by the board of trustees of the association, and these grants have been approved. These funds will be used by the American Hospital Association in conjunction with personnel supplied by the U. S. Public Health Service. The Commonwealth Fund will finance the publication of the report of the Commission on Hospital Care. In addition to assistance in preparing hospital schedules, the staff of the new department of the association will assist states with advice and with exchange of information on developing satisfactory study methods. This permits the association to continue its interest in the general aims of the Hospital Survey and Construction Act as passed by the last Congress. Mr. Maurice J. Norby, director of research for the Commission on Hospital Care, has been appointed assistant director of the association in charge of this latest activity. Mr. Ronald B. Almack will devote full time to the project as research analyst. Acting as liaison officer between the association and the U. S. Public Health Service will be Dr. David B. Wilson, surgeon of the public health service. Clerical personnel of the Commission on Hospital Care which have been concerned with tabulating hospital schedules will be transferred to the association direction.

LATIN AMERICA

Health Activities in Latin America—*Brazilian Medical Institute Dedicated.*—The Brazilian Institute of the History of Medicine, founded Nov. 30, 1945 in Rio de Janeiro, was officially dedicated recently with special ceremonies in the Assembly Hall of the Ministry of Education and Public Health. Dr. Ernesto de Souza Campos, minister of education and public health and honorary president of the institute, opened the program. Other speakers include Dr. Ivolino de Vasconcellos, president of the institute, and Drs. Mendonca Castro, Pedro Nava and Aloysio de Castro. Dr. Alvaro Doria is the general secretary, and Dr. Paulo Dias da Costa is the director of publicity.

New Journals.—The *Archivos de Neuro-Psiquiatria* made its appearance with the June issue. This quarterly journal is the official organ of the Sanatorio Dr. Galigarcia, Kokoito, Los Pinos, Havana, Cuba.

Inter-American Congress of Radiology.—Nearly 300 reservations have been made for North American radiologists and their families who will attend the second Inter-American Congress of Radiology, which will be held in Havana, November 17-22. The block of rooms reserved at the Nacional, the headquarters hotel, have long since been disposed of. Additional reservations are being made at the Sevilla-Biltmore. Requests for hotel accommodations should be directed to Mr. Mac F. Cahal, secretary of the committee, in care of the American College of Radiology, 20 North Wacker Drive, Chicago 6. Delegates must arrange for air or rail transportation through their local travel agent. Special trains will be operated by the Illinois Central from Chicago and the Atlantic Coast Line from New York. Reservations for the Illinois Central should be made with Mr. J. C. La Combe, 140 South Dearborn Street, Chicago 3, and for the Atlantic Coast Line with Mr. R. S. Voight, 16 East 44th Street, New York 17. Reservations for special flights to be operated from Chicago and New York to Miami by Eastern Airlines may be made in Chicago at 120 South Michigan Avenue, Chicago 3, or in New York at Park Avenue and 42d Street, New York 17. All delegates will be forced to go via air from Miami to Havana and return. No steamship service will be available. Reservation forms for Pan American Airways may be obtained from Mr. Cahal. The weather in Havana in November will be warm. Spring clothes are decreed. Passports are not required.

Third Pan American Congress of Ophthalmology.—The Sociedad Cubana de Oftalmologia is planning for the next Pan American Congress of Ophthalmology in Havana in February 1948 under the auspices of the Cuban government. In view of the motions approved by the second Pan American Congress of Ophthalmology, recently held in Montevideo, regarding the necessity of adopting measures for the prevention of blindness, the wife of the president of the republic, Sra. Paulina Alsina Vda. de Grau, is presiding over a movement for the foundation of a League Against Blindness and the establishment of a hospital for the treatment of eye diseases among the poor, and protection for the blind. The work on the hospital has already begun, the foundation stone having been laid, and it is hoped that the building will be finished within a few months and functioning perfectly by the time the congress is held in Havana.

CORRECTION

Exophthalmos and Thyrotoxicosis.—Footnote 5 in the editorial on page 81 of THE JOURNAL, September 14, should read Mann, Ida: Exophthalmic Ophthalmoplegia and Its Relation to Thyrotoxicosis, *Am. J. Ophth.* **29**:6 (June) 1946.

Marriages

KENNETH MERRILL LYNCH JR., Charleston, S. C., to Miss Yvonne Winters of Webster, N. Y., in Baldwinsville, N. Y., July 27.

ERNEST HAROLD WILLIAMS, Rocky Mount, N. C., to Miss Mary Evelyn Dobbins of Townville, S. C., July 16.

FREDERICK GRAFF, Parkersburg, W. Va., to Miss Margaret Anz of Asheville, N. C., in Annapolis, Md., July 3.

CORNELIUS BENTON BURNS, Camden, S. C., to Mrs. Margaret Roper Major of New Orleans, July 10.

ABRAM PINSKY, Jersey City, N. J., to Miss Carolyn Betty Cheston of Rochester, N. Y., July 23.

Deaths

Robert Miles Fawcett, Pittsburgh; University of Pittsburgh School of Medicine, 1937; born in Pittsburgh on Nov. 20, 1912; member of the American Medical Association; began active duty in the medical corps of the U. S. Army as a first lieutenant in September 1942; attached to the 758th Tank Battalion; landed in Africa in November 1942; saw service in the North African, Italian, southern France and German campaigns; received the Bronze Star, two Croix de Guerre decorations, seven campaign stars and three arrow heads for D day landings; transferred to the 108th General Hospital in Paris shortly before returning to the United States; received his commission as captain during the Italian campaign; interned at the Western Pennsylvania Hospital; served residencies at the Indiana Hospital in Indiana, Pa., and the Elizabeth Steel Magee Hospital, where he died July 27, aged 33, of massive coronary occlusion.

Marion Trueheart ✦ Sterling, Kan.; Kansas City Medical College, 1904; member of the House of Delegates of the American Medical Association in 1911, American Urological Association, Radiological Society of North America, American College of Radiology and the American Radium Society; fellow of the American College of Surgeons; specialist certified by the American Board of Radiology; past president of the Kansas Medical Society; served during World War I; medical superintendent of the Sterling Hospital; director of the First National Bank; died July 11, aged 65, of heart disease.

Gail Darwin Allee ✦ St. Louis; Beaumont Hospital Medical College, St. Louis, 1898; for many years affiliated with various Veterans Administration facilities; found dead in bed July 30 in Petoskey, Mich., aged 69, of coronary thrombosis and carcinoma of the liver.

Calvin Atkins, Independence, Mo.; University Medical College of Kansas City, 1890; member of the American Medical Association; formerly city physician; served on the staff of the Independence Sanitarium and Hospital, where he died July 10, aged 85, of abscess of the right lung.

Charles A. Balkwill ✦ Grafton, Wis.; Western University Faculty of Medicine, London, Ont., Canada, 1907; died July 29, aged 61, of lobar pneumonia.

James J. Baron, Providence, R. I.; Yale University School of Medicine, New Haven, 1903; died in the Rhode Island Hospital July 26, aged 74, of arteriosclerotic heart disease.

Homer Henry Beck, Corning, Calif.; Jefferson Medical College of Philadelphia, 1910; member of the American Medical Association; past president of the Tehama County Medical Society; died July 21, aged 60, of coronary thrombosis.

Jack Bevil ✦ Hull, Texas; St. Louis College of Physicians and Surgeons, 1919; past president of the Liberty-Chambers Counties Medical Society; died in the Hotel Dieu Hospital, Beaumont, July 24, aged 66, of congestive heart failure.

Warren Joshua Bieber, Bethlehem, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1904; died July 22, aged 70, in an automobile accident.

John Wesley Bird, Sturgeon Bay, Wis.; Chicago Homeopathic Medical College, 1893; served during World War I; died in the Memorial Hospital July 7, aged 76, of carcinoma.

Andrew J. Butts, Cherokee, Okla. (licensed in Oklahoma under the Act of 1908); at one time mayor of Skiatook; member of the Tulsa County Draft Board during World War I; died July 18, aged 83, of diabetes mellitus.

Harrison Ayer Chase, Brockton, Mass.; Harvard Medical School, Boston, 1905; member of the American Medical Association; fellow of the American College of Surgeons; on the staff of the Goddard Hospital; died in Falmouth July 23, aged 68, of cerebral hemorrhage.

Robert Deward Clark ✆ Alton, Ill.; Emory University School of Medicine, Atlanta, 1928; member of the West Virginia State Medical Association; died in a hospital at Beckley, W. Va., July 12, aged 47, of coronary thrombosis.

Peter Timothy Conlan ✦ Los Angeles; John A. Creighton Medical College, Omaha, 1898; on the staffs of the Queen of Angels and Methodist hospitals; died July 15, aged 75, of cirrhosis of the liver.

Almon Havens Cooke ✦ Buffalo; University of the City of New York Medical Department, 1892; served as president of the board of the Millard Fillmore Hospital; died July 31, aged 74, of cerebral thrombosis.

Benjamin Hill Copeland, Shiloh, Ga.; Atlanta College of Physicians and Surgeons, 1900; member of the American Medical Association; died July 18, aged 79, of cerebral hemorrhage.

Gilbert S. Couch, Mount Carmel, Ill.; Eclectic Medical Institute, Cincinnati, 1897; member of the American Medical Association; served a term as coroner; died in the Gibson General Hospital, Princeton, Ind., July 16, aged 75, of pneumonia.

David Harmon Daniel ✦ Paintsville, Ky.; University of Louisville Medical Department, 1908; served during World War I; served on the school board for several terms; formerly owner of the Prestonburg General Hospital in West Prestonburg and the City View Hospital; died July 4, aged 68, of congestive heart disease.

W. S. Davis, Sharps Chapel, Tenn.; University of Tennessee Medical Department, Nashville 1895; died July 21, aged 78, of carcinoma of the stomach and intestine.

Clay M. Easter, Beckley, W. Va.; Baltimore Medical College, 1895; served in France during World War I; died in Baltimore July 6, aged 75, of bilateral bronchopneumonia and carcinoma of the right tonsillar region.

Oliver Watt Ellison ✦ Independence, Kan.; Kansas City Medical College, 1901; died in the Mercy Hospital July 12, aged 73, of cerebral hemorrhage and mesenteric thrombosis.

Shakir Elias Far, Quincy, Mich.; University of Illinois College of Medicine, Chicago, 1917; member of the American Medical Association; local health officer and member of the town council; on the staff of the Community Health Center in Coldwater; died July 18, aged 57, of coronary thrombosis.

Arthur Preston Flowers, Atlanta, Ga.; Atlanta College of Physicians and Surgeons, 1900; member of the American Medical Association; died in the Crawford W. Long Hospital July 14, aged 70, of coronary occlusion.

George L. Garner, Santa Monica, Calif.; Detroit College of Medicine, 1886; died July 5, aged 89.

Joseph Harper Gaston ✦ Columbus, Ga.; Emory University School of Medicine, Atlanta, 1923; on the staff of the City Hospital; died July 15, aged 46, of heart disease.

Henry Greenberg, New York; Long Island College Hospital, Brooklyn, 1921; medical superintendent of the New York City Hospital; formerly medical director of the Morrisania City and Fordham hospitals; died July 23, aged 48, of coronary thrombosis.

Georg Krohn Gulck, Baltimore; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1928; medical missionary, American Lutheran Mission, Monrovia, Liberia, West Africa, from 1929 to 1946; died July 23, aged 50, of carcinoma of the colon.

Frederick Legro Hayes ✦ Brookline, Mass.; Jefferson Medical College of Philadelphia, 1895; associate medical examiner for Norfolk County; died in Wells Beach, Maine, July 6, aged 76, of heart disease.

LeRoy Frank Hollis, Lacona, N. Y.; Albany Medical College, 1893; member of the American Medical Association; served as health officer; for many years superintendent of the Oswego County Sanatorium, Richmond; died in the Oswego Hospital July 13, aged 75, of carcinoma of the prostate.

George Beam Hunt, Richmond, Ind.; Indiana University School of Medicine, Indianapolis, 1910; served overseas during World War I; secretary of the city board of health; formerly on the staff of the Reid Memorial Hospital; a charter member of the Kiwanis Club; died July 22, aged 64, of carcinoma of the liver.

Edward Henry Johnston ✦ Chicago; Loyola University School of Medicine, Chicago, 1918; died July 25, aged 53, of arteriosclerotic heart disease.

Frank Talbot McCormick ✦ Detroit; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1905; served as vice president and president of the Michigan Association of Industrial Physicians and Surgeons; died July 26, aged 66, of coronary occlusion.

Clifford Edward McElwain, Syracuse, N. Y.; Syracuse University College of Medicine, 1918; specialist certified by the American Board of Anesthesiology; member of the American Medical Association and the American Society of Anesthetists; instructor in clinical surgery (anesthesiology) at his alma mater; served during World Wars I and II; a member and past president of the medical staff of the Memorial Hospital; died July 20, aged 51, of coronary disease.

Alexander L. Martin Jr., Richmond, Va.; Medical College of Virginia, Richmond, 1928; member of the American Medical Association; died July 17, aged 43, of cirrhosis of the liver and nephritis.

Fernando C. Mock ✦ Milwaukee; Wisconsin College of Physicians and Surgeons, Milwaukee, 1898; died in the Mount Sinai Hospital July 12, aged 78, of empyema and arteriosclerosis.

V 132
1946

Alva Blake Mulvany, Kansas City, Mo.; University Medical College of Kansas City, 1904; member of the American Medical Association; formerly owner of the Industrial Hospital; died July 29, aged 66, of coronary occlusion.

Carroll Davis Overton, Hammond, La.; Tulane University of Louisiana School of Medicine, New Orleans, 1927; was shot and killed July 1, aged 43, by a former patient.

Edward E. Paddock, Kansas City, Mo.; Kansas City Medical College, 1895; died July 23, aged 79, of generalized arteriosclerosis.

James L. Ranes, Jacksonville, Ill.; Barnes Medical College, St. Louis, 1905; on the staff of the Jacksonville State Hospital; died in the Passavant Hospital July 17, aged 72, of coronary occlusion.

Robert Kline Rosenberger ✠ Schenectady, N. Y.; Medico-Chirurgical College of Philadelphia, 1909; named first surgeon for the city fire department Jan. 10, 1930, serving continuously since then; for many years on the staff of the City Hospital; died in the Ellis Hospital July 7, aged 62, of chronic glomerular nephritis.

James F. Schofield, Portage, Pa.; Baltimore University School of Medicine, 1893; for many years member of the local board of health and the Portage Council; at one time physician for the Huntingdon County Home for the Poor and the Friends' Home; died in the Conemaugh Valley Memorial Hospital, Johnstown, July 12, aged 76, of intestinal obstruction.

Henry Howard Schwartz, Los Angeles; Kansas City (Mo.) University of Physicians and Surgeons 1919; died June 22, aged 50.

William Mastin Scott ✠ Shreveport, La.; Tulane University of Louisiana School of Medicine, New Orleans, 1923; fellow of the American College of Physicians; died July 21, aged 46, of coronary occlusion.

John Kiyoshi Shima, Joliet Ill.; Tulane University of Louisiana School of Medicine, New Orleans, 1939; member of the American Medical Association; resident in radiology at Cook County Hospital, Chicago; served an internship and residency at the St. Joseph Hospital, where he died July 31, aged 34, of virus pneumonia.

Charles Franklin Stacey ✠ Blue Hill, Maine; Harvard Medical School, Boston, 1892; also a graduate in pharmacy; member of the Massachusetts Medical Society; died July 18, aged 79, of carcinoma of the esophagus.

LIEUT. EDWIN R. NELSON
(MC), U.S.N.R., 1908-1944

Rufus Webster Terhune, Martinsville, Ind.; Kentucky School of Medicine, Louisville, 1891; member of the American Medical Association; past president and secretary of the Johnson County Medical Society; served as postmaster of Whiteland and coroner of Johnson County; formerly on the staff of the Home Lawn Mineral Springs; died in Indianapolis July 28, aged 77, of cerebral hemorrhage.

Edward Arthur Tobin, North Bennington, Vt.; University of Vermont College of Medicine, Burlington, 1905; member of the American Medical Association; died June 19, aged 72, of coronary heart disease.

Charles Wesley Tyler, Polk City, Iowa; Drake University Medical Department, Des Moines, 1893; American Medical College, St. Louis, 1896; member of the American Medical Association; for many years a member of the school board; a director and president of the Polk City Savings Bank; died July 6, aged 77.

Austin Leroy Ward, Onalaska, Wash.; University of Minnesota Medical School, Minneapolis, 1900; died June 4, aged 73.

Edward James Wheatley, Baltimore; Howard University College of Medicine, Washington, D. C., 1898; died in the Atlantic City Hospital, Atlantic City, N. J., July 27, aged 74, of coronary thrombosis.

CAPTAIN JOSEPH L. NOCENTINI
M. C., A. U. S., 1910-1945

Alexander Lafayette White, Thomasville, Ala.; Memphis (Tenn.) Hospital Medical College, 1898; member of the American Medical Association; one of the founders and past president of the Clarke County Medical Society; died in Tuscaloosa July 19, aged 80, of arteriosclerosis.

James Pascal Wilson, Buffalo; University of the City of New York Medical Department, New York, 1889; member of the American Medical Association; died July 18, aged 84, of carcinoma of the larynx and tongue.

George Brown Woods, Washington, Pa.; University of Wooster Medical Department, Cleveland, 1874; member of the American Medical Association; for many years physician to the Washington County Home and Poor Farm; died July 24, aged 95, of senility.

Granville Mobi Wright, Toledo, Ohio; Long Island College Hospital, Brooklyn, 1898; member of the American Medical Association; served during World War I; died July 29, aged 75.

Henry Newton Yates, Meridian, Calif.; Eclectic Medical Institute, Cincinnati, 1891; died in Sacramento in July, aged 79, of arteriosclerosis.

KILLED IN ACTION

Edwin Robson Nelson, Huntington, W Va.; Medical College of Virginia, Richmond, 1936; diplomate of the National Board of Medical Examiners; member of the American Medical Association; interned at the State of Wisconsin General Hospital in Madison, where he served a residency in orthopedics; he also served a residency at the Logan General Hospital in Logan; beginning active duty with the grade of lieutenant (jg) in the medical corps, U. S. Naval Reserve, on Jan. 3, 1941, he was later promoted to lieutenant; killed in action in the Asiatic area Dec. 15, 1944, aged 36.

Joseph Louis Nocentini, Philadelphia; Temple University School of Medicine, Philadelphia, 1935; member of the American Medical Association; interned at the Conemaugh Valley Memorial Hospital in Johnstown, Pa.; served a residency at the Harlem Eye and Ear Hospital in New York; specialist certified by the American Board of Ophthalmology; member of the staff of the Wills Hospital; captain, medical corps, Army of the United States, serving as a flight surgeon in the African, Sicilian and Italian war theaters; aged 34; reported missing in action Jan. 12, 1944 while serving with the Eighth Troop Carrier Command in Italy; determined dead June 13, 1945.

132
946

Foreign Letters

LONDON

(From Our Regular Correspondent)

Sept. 8, 1946.

The Public Health During Six Years of War

During the war it was reported from time to time in THE JOURNAL that, excepting for the usual increase in venereal diseases and tuberculosis, the health of our population actually improved. Now it is possible to say more on this subject. A report of the chief medical officer of the Ministry of Health has just been published "On the State of the Public Health During Six Years of War." It tells of the public health and of the medical work during the trials of the grimmest struggle that Britain has endured. Vital statistics were phenomenally good. The birth rate, rising from 1941 onward, reached 17.7 per thousand of population in 1944, the highest since 1926 and within 1 per cent of the replacement standard, though it has fallen since. A feature was the low mortality of children from disease. Despite the loss of 7,000 lives at ages under 15 as a direct result of enemy action, and an increase of accidental deaths arising through war conditions, the mean annual deaths during 1940-1944 were below the rates for any year prior to 1939 at every age from 1 to 5 and at 5 to 9 and 10 to 14. The year 1939 was remarkable in low figures for mortality at every age group under 15 years. It was not expected that better figures would be obtained during the war, but new records for the second and third years of life were set up in 1942 and for the first, second, fourth and fifth years and at 5 to 9 years for 1942. The stillbirth rate declined continuously throughout the war, while successively low records for maternal mortality were established in 1940, 1942, 1943 and 1944. Considerable reductions in infant mortality rates occurred in the cities between 1938 and 1944. Thus there was a fall in London from 50 to 43 and in Manchester from 69 to 54. There was an increase in population at the ages most liable to fatal diseases, yet the period 1942-1944 showed reductions compared to the prewar years in a long list of causes of death, such as tuberculosis and pneumonia. During the war we escaped serious epidemics excepting for the occurrence of cerebrospinal meningitis, but its mortality was greatly reduced by new methods of treatment, which are estimated to have saved as many as 15,000 lives during the past five years. Two short epidemics of influenza, which were of a mild type, occurred.

The increase of early syphilis (counting civilians seen at the treatment centers and infections of British service men stated to have been contracted in this country) amounted to 140 per cent over the figures for 1939. There are greater difficulties in estimating the incidence of gonorrhea, but it is estimated that the increase was not so great, that it reached its peak in 1942, when it was probably 80 per cent higher than in 1939, and that in 1944 the percentage increase declined to 35. The problem of venereal diseases has been met by intensive propaganda on the importance of prompt treatment, the tracing of contacts and compulsory treatment of the recalcitrant spreaders of infection. Sulfonamides and penicillin have been most useful in reducing the period of infectivity.

Despite fatigue, monotony of diet and the restrictions of rationing, the nutritional state of the nation was maintained and, as regards children, seemed to be even better than before the war. This nutrition was the basis of the improved health of the population. The national loaf was improved by higher extraction of flour, and margarine was enriched by addition of vitamins A and D.

Homeopathic Hospitals Under the National Health Service

Homeopaths are concerned as to the position of their hospitals under the national health service. A deputation of the Homeopathic Association was received by the minister of health, Mr. Bevan. It stated that many people in all parts of the country wished to have homeopathic treatment, which should therefore be provided under the bill. To ensure that this demand was adequately met, the deputation asked that certain homeopathic hospitals should be designated as teaching hospitals under the bill, and that the homeopathic doctor should not be debarred from practice in an area on the ground that there was already a sufficiency of nonhomeopathic doctors.

In reply the minister of health said that homeopathic hospitals in general would come under the national health service scheme. He would try to preserve their special character and atmosphere, like that of other types of hospital, by making suitable appointments to the managing committees. But he thought that the regional hospital boards would have to look at the services in any given area before a conclusion could be arrived at as to any particular hospital. He could not give any assurance with regard to designating homeopathic hospitals as teaching hospitals. It was not his function to determine what kind of training was to be given in teaching hospitals; the university authorities must come into this question. There would be no discrimination against homeopathic methods; equally, of course, there would be no discrimination in favor of them or of any particular clinical methods. Many of these problems might not prove as formidable in practice as in theory, and he would be glad to ask the association to meet him again at a later stage when preparations were being made to bring the act into operation.

British Medical Journal Objects to the Dutch Starting an Abstracting Service in English

As reported previously in THE JOURNAL, the European nations are looking to Britain for the hegemony in medicine held by Germany before the war. A new example is the formation in the Netherlands of an abstracting medical service in the English language. This service is to issue a number of abstracting supplements in various special branches on lines similar to those of the German zentralblätter under the general title of Excerpta Medica. A distinguished group of Dutch medical men are associated with the work. The *British Medical Journal* announces that it would have felt more able to extend a welcome to this project but for two facts: the Dutch abstracting journals will be published in the English language and in ignorance of the project the *British Medical Journal* has, as previously reported here, established an abstracting service in its journal. Though flattering to this country and a recognition of the possibility that English will replace German as the second language of medical and scientific men, it is regrettable that our Dutch colleagues did not first inquire whether any British attempt was being made on a systematic scale to fill the gap left by the disappearance of the zentralblätter. However excellent may be the linguists at the disposal of our Dutch colleagues, the *British Medical Journal* thinks it unlikely that they can provide medical readers in Europe with a version in the English language up to the standards of British medical periodicals and that it is a pity that two competing abstracting services should be launched at the same time.

The First Woman Professor of Pathology

Miss Dorothy Russell has been appointed to succeed Professor Hubert Turnbull as director of the Bernhard Baron Institute of Pathology at the London Hospital. Professor Turnbull has retired after forty years' service. Miss Russell has also been appointed professor of morbid anatomy by London University. She is the first woman to be appointed to the senior staff of the London Hospitals as well as the first woman to be appointed professor of pathology in this country.

V 132
1946

BUENOS AIRES

(From Our Regular Correspondent)

July 21, 1946.

Improved Medical Care

General Juan D. Peron, president of Argentina, in a recent address to the deputies, said that his program includes such improvements in the field of medicine as the construction of hospitals, the equitable distribution of physicians and medical facilities in urban and rural zones, partial socialization of medicine and free medical care (not only for the poor, as it is given now, but also for families of moderate means). There will be 122,000 beds available in hospitals. Patients under this plan will select the physician they want. Well to do patients will have private medical care. The relations between these patients and the medical profession will be based on the rights of free practice.

Nutrition in Bolivia

An Argentine committee with Dr. Pedro Escudero, the head of the Instituto Nacional de Nutrición of Buenos Aires, Dr. Pedro Alberto Escudero Jr. and Dr. Arturo Leon López was recently appointed to study nutrition in Bolivia, which is deficient. The daily individual intake of proteins is only 40 Gm. Only 12 per cent of proteins are of animal origin. The main factors of deficient nutrition in Bolivia are the depreciation of Bolivian money and the need of importing food because of insufficient national production.

Taxes for National Health

The amount of taxes from clubs and balnearies on the Atlantic during 1945 and 1946 is 20,000,000 Argentine pesos ($5,000,000). The government distributed this amount for work in public health, urbanization, touring and social assistance as follows: Buenos Aires province 10,000,000 Argentine pesos ($2,500,000), National Department of Public Health 6,000,000 pesos ($1,500,000), and Secretariat of Work and Social Assistance 4,000,000 pesos ($1,000,000).

Society Reunion

At a recent meeting of the Academia Nacional de Medicina Dr. Eduardo L. Capdehourat of the Facultad de Medicina of the Universidad Nacional reported experiments and clinical, bacteriologic and x-ray observations in cases of abscess of the lung. A group of patients had sulfonamide nebulizations and intrapulmonary (intra-abscess) injections of the drug. A second group had intra-abscess injections of a mixture of the patient's own blood and emetine. The Castex-Capdehourat steel lung was shown. The apparatus synchronizes thoracic and abdominal respiration of the patient and makes it possible to obtain roentgenograms and electrocardiograms without moving the patient.

Dr. Egidio S. Mazzei, professor of the Universidad de la Plata, reported experiments carried out with Dr. Mario Dryer. Experimental pneumonia was obtained in animals after an injection into the respiratory tract of olive oil. Microscopic study of the lung of the animals confirmed the presence of pneumonia. The experiments indicated the development of pneumonia in children who swallow kerosene or choke when drinking milk, castor oil or cod liver oil and after the fat substances come in contact with the respiratory tract. The experiments showed also the danger of applying nasal drops in oil to children. The drug for nasal drops should be diluted in isotonic solution of sodium chloride.

Drs. Mazzei and Remolar reported experiments on dogs which have on the bronchi a mechanism with a valve through which air passes into the lung but not out of it. Experimental emphysema resulted. Dr. Mazzei reported studies on the blood, kidneys and hearts of dogs with experimental pulmonary emphysema.

Dr. Castex described a method for studying the human heart which he developed in collaboration with Drs. Antonio Battro and Hector Bidoglia. It consists in introducing a flexible sound through a vein in the arm and gently moving it up to the heart (either to the auricle or to the ventricle). The sound has within it a wire. When the sound reaches the heart the distal end of the wire is connected to an electrocardiograph, which produces an electrocardiogram from the heart itself. The process is said to be harmless to the patient. In some cases the sound was moved from the heart on through the inferior vena cava to the kidney. This opens the possibility of studying hypertension in patients. When the sound is in the heart there is the possibility of withdrawing intracardiac blood for investigation. It also opens the therapeutic possibility of injecting drugs through the sound into the heart.

Dr. Alfredo Di Ció reported results of experiments and clinical observations on the treatment of gangrene of the limbs with a mixture of carbon dioxide and oxygen at 5 per cent concentration. The treatment renders amputation unnecessary in cases of intermittent claudication.

Brief Items

Dr. Ramón Carrillo, professor of neurosurgery at the Facultad de Ciencias Médicas de Buenos Aires, was recently appointed secretary to the Secretariat of Public Health.

An Association of Universities of the United States and Argentina was recently established, with Dr. C. Taquini the president. The aims are to establish relations between teachers and university graduates of both countries, the opening of facilities for the same persons to carry on studies at universities, and to create and give scholarships. Also a center of scientific exchange for teachers, graduates and students of American and Argentine universities was recently established.

Dr. Oscar Ivanissevich was recently appointed ambassador from Argentina to the United States.

The Academia Nacional de Medicina has appointed Dr. Eduardo Braun Menendez, professor of physiology, a titular member, Drs. Alexander Fleming of London, Howard Walter Florey of Oxford and Gustavo Roussy of Paris honorary members, and Drs. U. S. von Euler of Stockholm, Ernst Laqueur of Amsterdam, Lucien de Gennes of Paris and Manuel Arroyo of Guatemala corresponding members.

Dr. José Valls, Professor of Orthopedics, was recently appointed president of the Asociación Médica Argentina, and Dr. Eduardo L. Capdehourat president of the Sociedad de Medicina Interna.

Dr. Ernst Laqueur, professor of pharmacology at Amsterdam, recently read papers at the Academia Nacional de Medicina and the Instituto de Fisiología on "Action of Male Hormones on Sex" and "Correlation Between Gonadotropins and Sex Hormones."

Dr. Gunnar Fischer of the Instituto Karolino of Stockholm recently lectured at the Instituto de Higiene of the Facultad de Ciencias Médicas of Buenos Aires on "Organization of Social Medicine in Sweden."

Dr. Amadeo Herlitzka, professor of physiology at the University of Turin, Italy, recently returned to Italy from Buenos Aires.

Dr. Oscar Riddle, an American endocrinologist and biologist, is visiting Latin America. He recently spent two months in Argentina and gave lectures in the Faculties of Medicine of Buenos Aires, Cordoba and other universities. He is now in Chile.

Dr. Avelino Gutiérrez of Buenos Aires died recently at the age of 82.

Correspondence

STREPOGENIN

To the Editor:—In an editorial with this title in THE JOURNAL, July 6, you reviewed the most interesting work of Dr. Woolley and his associates on their discovery of new non-identified nutritional substance for bacteria in certain protein materials.

Apparently Dr. Woolley has not been aware of the fact that my collaborator, Dr. Freedman, and I were very much on the same subject in the years 1920-1923. As a matter of record, the same subject was the basis of Dr. Louis Freedman's thesis in Columbia University College of Physicians and Surgeons in 1922. Aside from these facts a difference of conception is apparent between our early work and that of Dr. Woolley, which is well worth recording.

While Dr. Woolley is of the opinion that strepogenin is an integral part of certain proteins, our conception on the contrary was (Nutritional Factors in the Growth of Yeasts and Bacteria: I. Vitamins, II. Protein Hydrolysates, *J. Metabolic Research* **1**:457 [April] 1922; *Proc. Soc. Exper. Biol. & Med.* **19**:198, 1922) that the substance was of vitamin nature and was merely adsorbed on proteins derived from vitamin rich sources. This concept could be substantiated by a large number of proteins tested from various plant and animal sources. In fact, the substance was termed vitamin D, but unfortunately the opinion of Dr. E. V. McCollum at that time prevailed that substances required by micro-organisms should not be termed vitamins.

Finally, the better to prove our point, casein was transformed into sodium caseinate and the solution thus obtained treated with fullers' earth (Funk, Casimir; Paton, Julia B., and Freedman, Louis: *J. Metabolic Research* **3**:1 [Jan.] 1923). The casein reprecipitated from the filtrate was found completely inadequate for the nutrition of rats. In fact, we later suggested that this or a similar procedure is the only way to render casein really vitamin free. It has to be noted that the substance described by us was not destroyed by acid hydrolysis and that the fact that Woolley used crystalline proteins does not preclude a vitamin contamination by this highly absorbent material.

CASIMIR FUNK, New York.

FAILURE OF INTERSTATE QUARANTINE AGAINST POLIOMYELITIS

To the Editor:—In connection with the current discussion of the use of interstate quarantine to prevent the spread of poliomyelitis, the experience of one who witnessed its failure during the epidemic of 1916 may be of interest.

In the early days of that epidemic an official conference was called in Washington of state health officers and the Surgeon General and other officers of the United States Public Health Service to determine what had best be done. A draft of supposedly model interstate quarantine regulations was formulated, adopted by the conference and recommended for adoption by the several states. The vote in favor of adoption was, as I recall, unanimous, except that I, then health officer of the District of Columbia, refused to concur. Adoption by the several states, at least in the eastern part of the United States, where the disease was most prevalent, was prompt and general. The District of Columbia, however, could find no grounds that would justify it in joining the movement.

In the states that participated, quarantine officers were stationed at points of entry and departure of travel along interstate lines by rail, water, bus and private vehicle; permits to pass were required. Vehicles such as automobiles were frequently emptied of their occupants and searched to make sure that no children were hidden under robes or in the baggage compartment. The proceeding not only greatly inconvenienced the public and caused substantial expense but also aroused the already alarmed public to a greater pitch of excitement. The situation did not differ materially from that presented by interstate quarantine against yellow fever in the days of shotgun quarantine except that it had the sanction of law and shotguns were absent. But the District of Columbia, despite its usual large floating population, would have none of it. No passes were required to enter. None were required to leave; passes were issued to departing travelers only on request and to facilitate their passage through other jurisdictions. Incoming travelers were not inspected. Reliance for protection against the spread of the disease was placed on a few regulations promulgated in 1911. The grounds on which the District of Columbia rejected the regulations recommended by the conference of state health officers with the officers of the United States Public Health Service can be found in the Annual Report of the Health Officer of the District of Columbia for the Year Ending June 30, 1917, pages 12-15.

"Results," said the health officer in the report just cited, "fully justified the judgment of the health officer with respect to the situation, and on May 3, 1917 the Conference of State and Provincial Boards of Health, composed of men who in the preceding year most actively worked for the promulgation and enforcement of regulations of the most drastic type, adopted a report of its committee on methods for the control of infantile paralysis which in every way sustained the action taken by the health officer of the District during the preceding year."

If anything has developed in our knowledge of poliomyelitis since the epidemic of 1916 to excuse or justify interstate quarantine for its prevention, it has not come to my notice.

WILLIAM C. WOODWARD, M.D., Washington, D. C.

Medical Motion Pictures

INTERDEPARTMENTAL COMMITTEE FOR THE COORDINATION OF MEDICAL TRAINING FILM PRODUCTION

The War and Navy Departments, the U. S. Public Health Service and the Veterans Administration, realizing the proved value of films and film strips in the training of those who are interested in the field of medicine, have by cooperative effort established an Interdepartmental Committee for the Coordination of Medical Training Film Production.

This committee will develop production facilities and programs in an orderly and balanced manner and eliminate unnecessary duplication of effort. The committee at regular meetings discusses and decides on essential aspects of films or other training aids in production, films or other training aids urgently needed and the agency which possesses facilities essential to the production of a new project.

All visual aids planned and produced are being classified under a limited number of headings, each representing a general field of knowledge pertinent to medicine. Certain agencies possess facilities and subject material suitable for each field of knowledge referred to; hence the appropriate agency is designated in each instance to produce the aid required. Any agency which contemplates departure from this general plan brings the matter to the attention of the committee, and an appropriate solution to the problem is agreed on by all members.

It is further the desire of all concerned to make available in the future for loan to medical schools, medical groups, individual physicians and those engaged in activities considered a part of medical service, who are bound by professional ethics, motion pictures and other visual aids as far as it is possible within the legal limits imposed on each visual aid produced.

Ralph Creer of the Committee on Medical Motion Pictures, American Medical Association, attended a conference of the Interdepartmental Group in Washington on September 12.

V 132
1946

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

NATIONAL BOARD OF MEDICAL EXAMINERS EXAMINING BOARDS IN SPECIALTIES

Examinations of the National Board of Medical Examiners and the Examining Board in Specialties were published in THE JOURNAL, September 28, page 239.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: *Examination.* Montgomery, Jan. 21-23. Secretary, State Board of Medical Examiners, B. F. Austin, M.D., 519 Dexter Ave., Montgomery.

ARKANSAS: * Little Rock, Nov. 7-8. Sec., Medical Board of the Arkansas Medical Society, Dr. L. J. Kosminsky, Texarkana. *Eclectic.* Little Rock, Nov. 7. Sec., Dr. C. H. Young, 1415 Main St., Little Rock.

CALIFORNIA: *Examination.* Sacramento, Oct. 21-24. Secretary, Board of Medical Examiners, Dr. Frederick N. Scatena, 1020 N. Street, Sacramento.

CONNECTICUT: * *Examination.* Hartford, Nov. 12-13. Sec., Dr. Creighton Barker, 258 Church St., New Haven. *Homeopathic.* Derby, Nov. 12-13. Sec., Dr. J. H. Evans, 1488 Chapel St., New Haven.

DELAWARE: *Examination.* Dover, Jan. 14-16. *Endorsement.* Dover, Jan. 21. Sec., Medical Council of Delaware, Dr. J. S. McDaniel, 229 S. State St., Dover.

FLORIDA: * *Examination.* Jacksonville, Nov. 26-27. Sec., Dr. Harold D. Van Schaick, 2736 S.W. 7th Ave., Miami 36.

GEORGIA: Atlanta, Oct. 8-10. Sec., State Examining Boards, Mr. R. C. Coleman, 111 State Capitol, Atlanta 3.

HAWAII: *Examination.* Honolulu, Jan. 13-16. Secretary, Board of Medical Examiners, Dr. S. E. Doolittle, 881 S. Hotel St., Honolulu.

IDAHO: *Examination.* Boise, Jan. 14. Director, Board of Medical Examiners, Mrs. Agnes Barnhart, Room 355, State House, Boise.

ILLINOIS: Chicago, Oct. 15-17. Sec., Dept. of Registration & Education, Mr. Philip Harman, Springfield.

INDIANA: *Examination.* Indianapolis, June. Exec. Secretary, Board of Medical Registration and Examination, Miss Ruth V. Kirk, 627 K. of P. Bldg., Indianapolis.

KANSAS: Kansas City, Dec. 4-5. Secretary, Board of Medical Registration and Examination, J. F. Hassig, M.D., 905 North 7th Street, Kansas City.

KENTUCKY: *Examination.* Louisville, Dec. 16-18. Sec., State Board of Health, Dr. P. E. Blackerby, 620 S. Third St., Louisville 2.

MAINE: Portland, Nov. 12-13. Sec., Board of Registration of Medicine, Dr. A. P. Leighton, 192 State St., Portland.

MARYLAND: *Examination.* Baltimore, Dec. 10-13. Sec., Dr. E. H. Kloman, 1215 Cathedral St., Baltimore 1. *Homeopathic.* Baltimore, Dec. 10-11. Sec., Dr. J. A. Evans, 612 W. 40th St., Baltimore.

MASSACHUSETTS: *Examination.* Boston, Nov. 19-22. Sec., Board of Registration of Medicine, Dr. H. Q. Gallupe, 413-F State House, Boston 33.

MICHIGAN: * *Examination.* Lansing, Oct. 9-11. Sec., Board of Registration in Medicine, Dr. J. E. McIntyre, 100 W. Allegan St., Lansing 8.

MINNESOTA: * Minneapolis, Oct. 15-17. Sec., Dr. J. F. Du Bois, 230 Lowry Medical Arts Bldg., St. Paul 2.

MISSISSIPPI: *Reciprocity.* Jackson, Dec. Asst. Sec., State Board of Health, Dr. R. N. Whitfield, Jackson 113.

MISSOURI: *Examination.* St. Louis, Oct. 28-30. Dir., Medical Licensure, State Board of Health, Mrs. Lucy Motley, State Capitol Bldg., Jefferson City.

NEBRASKA: * *Examination.* Omaha, June 1947. Director, Bureau of Examining Boards, Mr. Oscar F. Humble, State Capitol Building, Lincoln.

NEVADA: *Examination.* Carson City, Nov. 4. Secretary, Board of Medical Examiners, Dr. G. H. Ross, 215 N. Carson St., Carson City.

NEW JERSEY: *Examination.* Trenton, Oct. 15-16. Sec., Dr. E. S. Hallinger, 28 W. State St., Trenton.

NEW MEXICO: * Santa Fe, Oct. 7-8. Sec., Dr. LeGrand Ward, 141 Palace Ave., Santa Fe.

NEW YORK: *Examination.* Albany, Buffalo, New York & Syracuse, Oct. 7-10. Sec., Dr. Jacob L. Lochner, Education Bldg., Albany.

NORTH CAROLINA: *Examination.* Winston-Salem, Dec. 16-19. *Endorsement.* Dec. 17. Act. Sec., Mrs. L. McNeill, 226 Hillsboro St., Raleigh.

NORTH DAKOTA: Grand Forks, Jan. 7-10. Secretary, Dr. G. M. Williamson, 4½ S. Third St., Grand Forks.

OHIO: *Examination.* Columbus, Dec. 3-5. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus.

OREGON: * *Examination.* Portland, Jan. *Reciprocity.* Portland, Oct. 26. Exec. Sec., Miss L. M. Conlee, 608 Failing Bldg., Portland 4.

PENNSYLVANIA: *Examination.* Harrisburg, Oct. Act. Sec., Bureau of Professional Licensing, Dept. of Public Instruction, Mrs. M. G. Steiner, 351 Education Bldg., Harrisburg.

SOUTH CAROLINA: Columbia, Nov. 11-12. Sec., Dr. N. B. Heyward, 1329 Blanding St., Columbia.

SOUTH DAKOTA: * *Examination and Reciprocity.* Vermillion, Jan. 21-22. Secretary, Board of Medical Examiners, Dr. Gilbert Cottam, State Capitol Building, Pierre.

TEXAS: *Examination.* Oct. 31-Nov. 2. Sec., Dr. T. J. Crowe, 918-20 Texas Bank Bldg., Dallas 2.

VERMONT: *Examination.* Burlington, Jan. 31-Feb. 1. Secretary, Board of Medical Registration, Dr. F. J. Lawliss, Richford.

VIRGINIA: Richmond, Dec. 3-6. Secretary, Board of Medical Examiners, Dr. J. W. Preston, 30½ Franklin Rd., Roanoke.

WASHINGTON: *Examination.* Seattle, Jan., 1947. Secretary, Mr. Nelson Vaughn, Olympia.

WEST VIRGINIA: Charleston, Oct. 7-9. Commissioner, Public Health Council, Dr. N. H. Dyer, State Capitol, Charleston 5.

WYOMING: *Examination.* Cheyenne, Oct. 7-8. Sec., Dr. G. M. Anderson, Capitol Bldg., Cheyenne.

* Basic Science Certificate required.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ARIZONA: Dec. 10. Sec., Mr. Francis A. Roy, Science Hall, University of Arizona, Tucson.

CONNECTICUT: *Examination.* New Haven, Oct. 12. Exec. Asst., State Board of Healing Arts, Mr. W. G. Reynolds, 250 Church St., New Haven.

DISTRICT OF COLUMBIA: *Examination.* Washington, Oct. 21-22. Sec., Commission on Licensure, Dr. G. C. Rubland, 6150 E. Municipal Bldg., Washington.

FLORIDA: *Examination.* Gainesville, Nov. 2. Sec., Dr. J. F. Conn, John B. Stetson Univ., Deland.

IOWA: *Examination.* Des Moines, Oct. 8. Corresponding Sec., Division of Licensure & Registration, Mr. H. W. Grefe, Capitol Bldg., Des Moines 19.

MICHIGAN: *Examination.* Ann Arbor, Oct. 11-12. Sec., Miss Eloise LeBeau, 101 N. Walnut St., Lansing.

NEW MEXICO: *Examination.* Nov. 3. Sec., Miss Marion M. Rhea, State Capitol, Santa Fe.

OREGON: *Examination.* Portland, Nov. 2. Sec., Mr. C. D. Byrne, Univ. of Oregon, Eugene.

RHODE ISLAND: *Examination.* Providence, Nov. 13. Chief, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

SOUTH DAKOTA: Sioux Falls, Dec. 6-7. Sec., Dr. G. M. Evans, Yankton.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Food and Drug Acts: Federal; Coal Tar Colors Not to Be Used for Eyebrow Dye.—The plaintiff, doing business as Nu-Charme Laboratories, marketed a quantity of Nu-Charme Perfected Brow Tint which was seized by the government on the ground that it contained a poisonous and delcterious substance. From a summary judgment ordering destruction of the property seized, the plaintiff appealed to the circuit court of appeals, fifth circuit.

It was undisputed that the preparation contained "paraphenylene diamine," the coloring derived from coal tar, and the Federal Security Administrator has banned the use of such colors in preparations applied in the orbital area. The plaintiff insists that his product is not injurious to users under the conditions prescribed in the labeling thereof and he questions the right of the administrator to ban the use of such colors under the circumstances.

Section 371 (e) of the food and drug act authorizes the administrator to hold public hearings after appropriate notice thereof is given. Such notice was given in this instance and published in the *Federal Register* as provided by law. It set forth the proposal in general terms and specified the time and place for the hearing to be held, which was not less than thirty days after the date of the notice. The hearing was had, findings of fact were made from evidence of record, and the regulation was duly promulgated. Evidence of the poisonous and pernicious effects liable to be caused by the application of any coal tar color to the orbital area was not controverted by direct and positive testimony of record. At the hearing the administrator found that coal tar colors are not harmless for use in preparations applied in the orbital area, which includes the eyebrows, the eyelids, the eyelashes, the conjunctival sac of the eye, the eyeballs and the soft areolar tissue that lies within the perimeter of the infraorbital ridge but rather that the application may cause serious injury and even loss of sight. Thereupon he issued the regulation that no coal tar color should be certified for use in a product to be applied in the area of the eye. Such quasi legislative action, said the court, was not arbitrary or capricious but was the reasonable exercise of a sound judgment and discretion.

The promulgating authority granted to the administrator is a quasi legislative power. He is given a wide discretion and his judgment, if based on substantial evidence of record and within statutory and constitutional limitations, is controlling even though the reviewing court might on the same record have arrived at a different conclusion. The statute contemplates that he shall not arbitrarily exercise his power but shall act only on a conscientious judgment derived from a consideration of the facts and conditions to which the regulation is to be applied. The regulation, the court said, was promulgated according to the policy set forth in the act; the necessary method prescribed was the listing of coal tar colors found to be harmless, and certification of batches of such colors; a standard was furnished in prescribing that the regulation would list only such colors as were found to be harmless and suitable for use. Congress stated the general rule and left to the administrator the duty of ascertaining what particular colors should be listed. This procedure, the court concluded, meets the test required by the due process clause of the Fifth Amendment. Accordingly the judgment ordering confiscation and destruction of the property seized was affirmed.—*Byrd v. United States, 154 F. (2d) 62 (1946).*

Current Medical Literature

AMERICAN

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Titles marked with an asterisk (*) are abstracted below.

American Journal of Ophthalmology, Cincinnati

29:785-926 (July) 1946

Scleral Resection (Eyeball Shortening) Operation. D. Vail.—p. 785.
*Retinal Hemorrhage as Seen in Atomic Bomb Casualty. K. B. Benkwith.—p. 799.
Effects of Vitamin A Deficiency on Eye of Rabbit. Ida Mann, A. Pirie, K. Tansley and C. Wood.—p. 801.
Management of Intraocular Foreign Bodies in Military Practice. G. M. Haik.—p. 815.
Effect of Sunlight on Dark Adaptation. B. Clark, M. L. Johnson and R. E. Dreher.—p. 828.
Observations on Vossius Ring. T. Gundersen.—p. 837.
Saccular Prolapse of Vitreous Body: Report of Case. R. A. Poirier.—p. 845.
Cyclodialysis in Treatment of Glaucomas. S. D. McPherson Jr.—p. 848.
Unaided Visual Acuities Correlated with Refractive Errors: Study. M. H. Pincus.—p. 853.

Retinal Hemorrhage in Atomic Bomb Casualty.—A Japanese girl aged 14 years had retinal hemorrhages as a result of the atomic bomb explosion at Nagasaki. She was ambulatory, although she had earlier suffered from malaise, headache, fever, nausea and diarrhea. Later she noted petechiae in her skin, slight epilation, bleeding from the gums and blurred vision. She was approximately 1 mile from the accepted hypocenter of the atomic bomb explosion. Examination of the fundi early in September showed massive preretinal hemorrhage in each eye and hemorrhages into the fiber layer of the retina. In the macula of the left eye was a large sausage-shaped hemorrhage appearing to be fed by the terminal arterioles and venules of that region. Small fluffy white exudates were scattered about the disk and in close approximation to the retinal vessels of greater caliber. The ill effects of the excessive radiant energy gradually subsided, so that by November there was a definite clearing of the fundi. The retinal hemorrhages were absorbed faster than the whitish areas of apparent serofibrinous exudate, which also disappeared. Little evidence of pathologic change was visible in the fundi by December. A small white area persisted in the fundus of the left eye.

Archives of Internal Medicine, Chicago

77:597-726 (June) 1946

Amebiasis Among American Armed Forces in Middle East. E. J. Tallant and A. L. Maisel, with technical assistance of M. Ruth Rakestraw.—p. 597.
Thromboangiitis of Pulmonary Vessels Associated with Aneurysm of Pulmonary Artery: Report of Case. L. E. Thompson and B. Gerstl.—p. 614.
Acute Porphyria: I. Investigations on Pathology of Porphyrins and Identification of Excretion of Uroporphyrin I. F. T. G. Prunty.—p. 623.
Peripheral Blood Flow, Rectal and Skin Temperature in Congestive Heart Failure: Effects of Rapid Digitalization in This State. H. J. Stewart, W. F. Evans, Halla Brown and Jacqueline R. Gerjuoy.—p. 643.
*Patent Ductus Arteriosus with Subacute Bacterial Endarteritis: Diagnosis and Indications for Operation. H. Vesell and I. Kross.—p. 659.
Pneumonia in the Aged: Analysis of 166 Cases of Its Occurrence in Patients 60 Years Old and Over. F. D. Zeman and K. Wallach.—p. 678.
Allergy: Review of Literature of 1944 and 1945, with Comments on Future Problems. F. M. Rackemann.—p. 700.

Patent Ductus Arteriosus and Bacterial Endocarditis.—Vesell and Kross report a case in which patent ductus arteriosus and bacterial endocarditis were successfully treated with penicillin and surgical measures.

Archives of Otolaryngology, Chicago

43:549-682 (June) 1946

*Surgical Treatment of Otosclerosis: Preliminary Report on Improved Fenestration Technic. G. E. Shambaugh Jr. and A. L. Juers.—p. 549.
Late Secondary Tonsillar Hemorrhage: II. Studies of Ascorbic Acid. H. Neivert, L. A. Pirk and R. Engelberg.—p. 568.
Treatment of Tuberculosis of Larynx: Evaluation. W. F. Hulse.—p. 578.
Penicillin Ear Drops in Treatment of Suppurative Otitis Media. W. J. Loeb.—p. 586.
Hypertrophy of Masseter Muscle. J. H. Hersh.—p. 593.
Evaluation of Benadryl as Therapeutic Agent for Vasomotor and Allergic Rhinitis. E. A. Thacker.—p. 597.
Treatment of Chronic Purulent Otitis Media with Glycerite of Hydrogen Peroxide. E. A. Brown and W. E. Owen.—p. 605.
Atresia of External Auditory Canal Occurring in Military Service: Report on Correction of This Condition in 10 Cases. J. J. Conley.—p. 613.
Effect of Zephiran Chloride, Tyrothricin, Penicillin and Streptomycin on Ciliary Action. G. Greenwood, R. E. Pittenger, G. A. Constant and A. C. Ivy.—p. 623.
Advances in Understanding of Rhinologic and Otologic Conditions Related to Nervous System: Critical Survey of Literature. W. P. Eagleton.—p. 631.

Improved Fenestration Technic in Otosclerosis.—The new fenestration technic developed at Northwestern University departs from other technics in a number of ways, the most important of which are that (*a*) it assures enchondralization of the fistula, (*b*) it includes constant irrigation of the operative field and use of the microscope while the fistula is being made, (*c*) it scrupulously avoids traumatization of the endosteum within the labyrinth, (*d*) it places the fistula on the horizontal semicircular canal laterally and (*e*) it makes use of a sea sponge and head frame technic to prevent postoperative serous labyrinthitis, which has been the most frequent cause of failure since the measures to prevent bony closures were adopted.

Archives of Surgery, Chicago

52:619-744 (June) 1946

*Total Pancreatectomy for Carcinoma of Pancreas in Diabetic Person: Metabolic Studies. C. F. Dixon, M. W. Comfort, A. L. Lichtman and R. E. Benson.—p. 619.
Parenteral Administration of Fluids During Early Care of Battle Casualties. E. E. Muirhead, M. H. Grow and A. T. Walker.—p. 640.
Pulsating Benign Giant Cell Tumors of Bone: Report of Case and Review of Literature. T. A. Shallow and F. B. Wagner Jr.—p. 661.
Injection into Pericardial Sac and Ligation of Coronary Artery of Rat. R. F. Heimburger.—p. 677.
Pilonidal Sinus: Review of 130 Consecutive Cases in Which Patients Were Treated by Closure: New Closed Operative Method and Management. C. E. Pope and H. W. Hudson.—p. 690.
New and Successful Closed Operative Procedure for Pilonidal Sinus: Gluteus Maximus Mobilization: Sliding Muscle Graft Procedure. C. E. Pope.—p. 701.
Anaphylaxis-like Reactions Produced by Ascaris Extracts: II. Mechanism of Shock Induced in Dogs. M. Rocha e Silva and A. Graña.—p. 713.
Struma Lymphomatosa: Clinicopathologic Study. B. J. Ficarra.—p. 729.

Pancreatectomy for Carcinoma of Pancreas in Diabetic Person.—Total pancreatectomy was performed on a diabetic man aged 50 for carcinoma of the pancreas. Dixon and his co-workers studied the effect of the lack of internal and external secretions of the pancreas. Total pancreatectomy did not produce diarrhea in spite of the large amount of fat in the stools. About a half of the ingested fat and about a third of the ingested protein were lost in the feces. Digestion of fat was surprisingly good, as only about a third of the fat in the feces was neutral fat. The absorption of calcium and phosphorus was apparently adequate in spite of the high loss of foodstuffs in the stools. Concentrated pancreatin in enteric coated tablets (fifteen with each meal, or 15 Gm. daily) reduced the loss of fat and protein by approximately 50 per cent. It also reduced the dry weight of the feces and altered the gross appearance of the stool. Concentrated pancreatin reduced the loss of calories sufficiently to cause the patient to gain weight slightly. The amounts of fat and nitrogen lost in the feces even when pancreatin was given were in excess of normal values. Although concentrated pancreatin was not a complete substitute for external pancreatic secretion, it was valuable in maintaining the nutrition. Total pancreatectomy was not followed during the eight months of observation by a decrease in the amount of glucose lost in the urine or of the insulin requirements or by hypolipemia and hepatic dysfunction indicative of a fatty liver, as is often the case in pancreatectomized dogs. On the contrary, the patient's diabetes remained about the same, the pro-

V 132
1946

tamine zinc insulin requirement being approximately 40 units a day. Hepatic function remained unimpaired, and hyperlipemia rather than hypolipemia appeared. The patient remained in good health and maintained his weight while taking a mixed diet plus insulin and 10 Gm. of concentrated pancreatin. His condition was good twelve months after operation.

Journal of Infectious Diseases, Chicago

78:173-258 (May-June) 1946

Studies on Malarial Parasites. J. W. Ferrebee and Q. M. Geiman.—p. 173.
Study of Survival of Certain Strains of Viruses After Lyophilization and Prolonged Storage. R. E. Hoffstadt and Helen B. Tripi.—p. 183.
Biochemistry of Malaria Parasite: IV. In Vitro Effects of X-Rays on Plasmodium Gallinaceum. J. Ceithaml and E. A. Evans Jr.—p. 190.
Bacteriology of Collection of Shigella Strains Types by Weil's Method. M. Fulton and Sylvia F. Curtis.—p. 198.
Instability of Agglutinative Reaction in Beta Hemolytic Streptococci of Group A. Alice C. Evans.—p. 204.
Protective Effects of Bacteria on Western Equine Encephalomyelitis Virus. Shih-Fan Chung.—p. 216.
Use of Antibiotics, Vitamin Analogues and Other Compounds in Experimental Gas Gangrene. F. J. Ryan, R. Ballentine, Lilian K. Schneider, Edith Stolovy, Mary E. Corson and Elizabeth J. Ryan.—p. 223.
Functional Antigens in Helminths. J. Oliver-González.—p. 232.
Photography of Airborne Particles During Bacteriological Plating Operations. K. R. Johansson and D. H. Ferris.—p. 238.
Action of Clavacin, A Clavacin Isomer and Related Compounds on Tetanus Toxin. B. Puetzer and T. C. Grubb.—p. 253.

Journal of Nervous and Mental Diseases, New York

103:549-726 (June) 1946

Motivation of Crime. D. Abrahamsen.—p. 549.
Scientific Proof and Relations of Law and Medicine: Simulation of Nervous and Mental Disease. M. Kesehner.—p. 571.
Integration of Medical Science and Sociology. A. W. Stearns.—p. 612.
Sexual Offenders. W. N. East.—p. 626.
Medicolegal Aspects of Spinal Cord Injuries. F. Kennedy and P. G. Denker.—p. 667.
Ruptured Intervertebral Disk. J. S. Barr and W. M. Craig.—p. 688.

Journal of Neurophysiology, Springfield, Ill.

9:263-346 (July) 1946

Electromyographic Studies of Muscular Coordination on Stimulation of Motor Cortex. J. F. Bosma and E. Gellhorn.—p. 263.
Centrifugal Deterioration of Asphyxiated Peripheral Nerve. R. A. Groat and H. Koenig.—p. 275.
Hypothalamic Regulation of Sleep in Rats: Experimental Study. W. J. H. Nauta.—p. 285.
Frequency of Centripetal Stimulation in Inhibition and Facilitation of Knee Jerk. Harriet M. Maling.—p. 317.
Mechanism of Pupillary Dilatation Elicited by Cortical Stimulation. A. A. Ward Jr. and H. L. Reed.—p. 329.
Inhibition at Nerve Muscle Junction in Crustacea. S. W. Kuffler and B. Katz.—p. 337.

New England Journal of Medicine, Boston

234:849-878 (June 27) 1946

Disputed Indications and Technics for Cesarean Section. E. G. Waters.—p. 849.
*Treatment of Bacterial Arthritis with Penicillin. H. L. Hirsh, H. L. Feffer and H. F. Dowling.—p. 853.
Three Years' Experience with Electric Convulsive Therapy. J. Norman and J. T. Shea.—p. 857.
Gynecology: Carcinoma of Vulva. L. Parsons and J. V. Meigs.—p. 860.
Generalized Hemochromatosis, Including Liver, Pancreas, Lymph Nodes, Thyroid and Pituitary Glands and Heart.—p. 866.
Actinomycotic Abscesses of Peritoneum and Liver, with Perforation of Right Diaphragm.—p. 870.

Penicillin in Bacterial Arthritis.—Hirsh and his associates employed penicillin in 26 patients with bacterial arthritis. Seventeen had gonococcic arthritis, 7 had staphylococcic arthritis and 1 each had arthritis caused by the hemolytic streptococcus and the pneumococcus. Successful results were obtained in acute gonococcic arthritis when penicillin was administered systematically in adequate doses and in arthritis caused by the staphylococcus, the hemolytic streptococcus and the pneumococcus when adequate amounts of penicillin were injected into the joint, accompanied by penicillin systematically in patients with extra-articular infection. The following dosage schedules are recommended: in acute gonococcic arthritis 25,000 units should be injected intramuscularly every three hours for at least five days, or longer if needed; in arthritis caused by the staphylococcus, the beta-hemolytic streptococcus or the pneumococcus, 30,000 to 50,000 units should be administered intra-articularly on alternate days until local and general signs of inflammation have disappeared. If extra-articular infection is present, penicillin should also be given intramuscularly in amounts of 25,000 units every three hours.

Southern Medical Journal, Birmingham, Ala.

39:527-596 (July) 1946

Neurosurgical Experiences in Lumbago-Sciatic Syndrome. E. F. Fincher.—p. 527.
History of Hemorrhoidal Surgery. C. J. Holley.—p. 536.
Spinal Anesthesia, with Special Reference to Use of Procaine-"Pontocaine" Mixture. C. E. Newell.—p. 542.
Aberrant Pancreas in Duodenum. J. C. Norris.—p. 549.
*Prevention and Control of Disturbances of Protein Metabolism in Rocky Mountain Spotted Fever: Value of Forced Feedings of High Protein Diet and of Administration of Specific Antiserum. G. T. Harrell, W. A. Wolff, W. L. Venning and J. B. Reinhart.—p. 551.
Selective Radiation Obtained by Intravenous Administration of Colloidal Radioactive Isotopes in Diseases of Lymphoid System. P. F. Hahn and C. W. Sheppard.—p. 558.
*Retention and Excretion of Manganese Dioxide Dispersions Administered Intravenously to Humans. C. W. Sheppard and P. F. Hahn.—p. 562.
Use of Radium and Roentgen Rays in Treatment of Hyperplastic Lymphoid Tissue in Nasopharynx and Pharynx. G. E. Fisher.—p. 565.
Roentgenologic Consideration of Gastrointestinal Disturbances, with Special Reference to Stomach and Duodenum. R. G. Giles.—p. 570.
Perforated Peptic Ulcers in Naval Personnel. Shirley C. Lyons and L. G. Sinclair.—p. 575.
Estrogenic Hormones, Often Only a Psychotherapeutic Agent. J. D. Weaver.—p. 581.
Management of Common Obstetric Complications in General Practice. H. L. Choate.—p. 585.
Progress Note on Medical Education in South Carolina. W. H. Kelley.—p. 588.

Protein Metabolism in Rocky Mountain Spotted Fever.—The administration of a high protein diet appears to be of value in the therapy of rickettsial spotted fever. The daily protein requirement seems to be in the range of 4 Gm. per kilogram of body weight. If this level is not obtained with a basic diet, supplementary feedings of a high protein liquid should be given by gavage if necessary. In 9 pediatric patients with rickettsial spotted fever treated during 1945 with a high protein intake the amount of edema and the amount of preformed proteins required for support of the circulation was reduced. Although blood protein levels, especially the albumin fraction, were only slightly better maintained, there appeared to be less depletion of body proteins, as measured by studies of the urinary nitrogen excretion. A potent specific antiserum seems to be useful in controlling the toxic symptoms if administration is begun before the third day of rash. Repeated full therapeutic doses, rather than a single injection, should be given daily or at two day intervals. The administration of specific antiserum did not prevent alterations in protein metabolism even in patients receiving an adequate protein intake.

Manganese Dioxide Dispersions Administered Intravenously.—Sheppard and Hahn think that in evaluating the therapeutic effect of colloidal manganese dioxide containing radioactive manganese it is important to know to what extent it is retained by the body after administration. Excretion studies were therefore made on 3 patients who had received therapeutic doses of radioactive manganese. Measurements were also made of the gamma ray intensity at selected locations over the body surface of these patients and several others. In 1 instance the gamma ray measurements were repeated on several successive dates in order to follow the decline of the activity in the patient's body. It was found that an appreciable fraction (about 5 per cent) of the initial dose is excreted through the bile immediately after administration. The body then retains the remainder, losing it at a low rate. The gamma ray intensity at the body surface is greatest near the region of the liver.

West Virginia Medical Journal, Charleston

42:171-194 (July) 1946

Patent Ductus Arteriosus. W. C. Stewart.—p. 171.
Solving Problem of Toxicity of New Chemicals in Industry. H. F. Smyth Jr.—p. 177.
Oxygen Treatment for Chlorine Gas Exposures. T. W. Nale.—p. 178.
Mustard Gas Burns—Clinical Experiences. E. L. Gage.—p. 180.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

Edinburgh Medical Journal

53:209-272 (May) 1946

Progress of Dermatology: Inaugural Address. G. H. Percival.—p. 209.
Anticoagulant Therapy in Thrombosis. J. E. Jorpes.—p. 222.
Meningococcemia: Part III. Bacteriology, Serology and Etiology. W. R. Logan.—p. 235.
Treatment of Cholera by Intravenous Saline Injections, with Particular Reference to Contributions of Dr. Thomas Aitchison Latta of Leith (1832). E. D. W. Greig.—p. 256.

Lancet, London

1:949-988 (June 29) 1946

Phenylketonuria: Problem in Eugenics. L. S. Penrose.—p. 949.
Pain of Organic Disease Relieved by Prefrontal Lobotomy. W. Freeman and J. W. Watts.—p. 953.
*Laboratory Diagnosis of Weil's Disease: Six Years' Observations. A. D. Gardner and J. A. H. Wylie.—p. 955.
Subacute Hepatic Necrosis Treated with Methionine: Successful Case. D. G. Ferriman, G. E. O. Williams and D. S. Cadman.—p. 958.
"Burning Feet" in British Prisoners of War in Far East. J. Simpson. —p. 959.
Nutritional Deficiency, Painful Feet, High Blood Pressure in Hong Kong.—p. 961.

Laboratory Diagnosis of Weil's Disease.—In the last six years Gardner and Wylie have examined 1,120 human serums, of which 182 have agglutinated a suspension of Leptospira icterohemorrhagiae in dilutions up to and greater than 1 in 400, the majority having a higher titer than 1 in 1,600. The technic used for the serum titrations has been a microscopic tube agglutination method using formolized serum water cultures of the organism. Although the chief diagnostic work carried out by the authors has been serologic, they have undertaken other diagnostic tests for leptospirosis: blood culture, dark ground examination of blood and urine, and guinea pig inoculation. These maneuvers usually have been unsuccessful. This is in part due to postal delays in the arrival of the specimens; but, owing to the poor viability of leptospiras outside the body, these measures even in the most favorable circumstances are less often successful than the titration of antibodies. The blood urea level has been raised, in many cases greatly. Evidence of renal damage should be sought in all suspected cases. In the experimental animal the renal lesion develops early and is a constant feature in contrast to the variation found in the hepatic involvement. In the human disease also too much emphasis has been laid on the hepatic aspect of this syndrome. Satisfactory as the agglutination test is for the diagnosis of Weil's disease after about five days, it does not adequately cover the very early stages.

Medical Journal of Australia, Sydney

1:753-788 (June 1) 1946

Clinical Lessons From Prisoner of War Hospitals in Far East (Burma and Siam). A. E. Coates.—p. 753.
Clinical Lessons From Prisoner of War Hospitals in Far East. E. E. Dunlop.—p. 761.
Observations by Pathologist During Three and Half Years as Prisoner of War in Malaya and Thailand. A. T. H. Marsden.—p. 766.
Medical Aspects of Singapore Captivity. C. Harvey.—p. 769.
Medical Experiences as Prisoner of War. N. H. Rose.—p. 772.
Experiences as Prisoner of War in Japan. S. E. L. Stening.—p. 773.
Surgical Experiences as Prisoner of War. K. J. Fagan.—p. 775.

1:789-824 (June 8) 1946

*Clinical Picture of Pappataci Fever, Especially in Palestine. A. Sandler. —p. 789.
Relationship of Food to Health. Mildred Hutchings.—p. 796.
Complications and Sequelae of Prophylactic Inoculations. M. Kelly. —p. 800.

Pappataci Fever.—Sandler reviews observations in 210 cases of sandfly fever (pappataci fever) among the students of the Hebrew University, Jerusalem. The symptoms manifested in these cases have been compared with those found by Walker and Dods in an Australian army hospital at Gaza and with symptoms described in the literature on pappataci fever in Palestine and elsewhere. Sandler's observations agree on the whole with those of Walker and Dods. Nearly all his patients complained of severe pain in the thigh, a symptom absent in the cases of Walker and Dods, who saw in almost all of them an enanthem of the palate rarely found by others. A comparison of the present series with others in different epidemics reveals the existence of considerable variations in the symptomatology of pappataci fever. The author feels that these variations are not determined by geographic factors but by the fact that pappataci fever has three or four different clinical forms, any of which may occur in the same country. Reviews of the subject are at variance with one another. No single review gives a true picture of the entire literature, but all authors seem more or less to have followed the descriptions of certain forms of the disease. Treatment is generally superfluous, the severe phase of fever being brief and the prognosis always favorable.

Acta Clinica Belgica, Brussels

1:197-288 (May-June) 1946

*Various Aspects of Atrophy of Pituitary Body. M. Herlant.—p. 197.
Gravimetric Determination of Hemoglobin. L. Brull.—p. 218.
Frequency of Development of Basophil Granules Except for Lead Poisoning. A. Lambrechts, A. Nizet, L. Lefevre and P. de Marchin.—p. 224.
Acute Crisis of Hypothyroxinemia Induced by Administration of Thiouracil. J. Mahaux.—p. 234.
Relationship Between 3 Cases of Cutaneous Hodgkin's Disease: Presentation of Moulages. L. Van Der Meiren.—p. 246.
Silicosis in Basin of Liège. A. Thomas.—p. 255.

Atrophy of Pituitary Body.—Herlant made a pathologic and clinical study of Simmonds disease in 3 women between the ages of 36 and 66 and a man aged 50 who were admitted to the St. Pierre Hospital in Brussels. The characteristic lesion associated with this disease is the destruction of the anterior lobe of the pituitary caused by a specific or nonspecific inflammation or by a solid or cystic tumor. The author agrees with Sheehan that in women the pituitary atrophy may usually be caused by a postpartum thrombotic necrosis, although this was not the fact in the patients presented. The destruction of the anterior lobe of the pituitary is followed by a secondary hypoplasia of the gonads, the thyroid and the adrenal cortex similar to the atrophy observed in animals after hypophysectomy. The clinical symptomatology varies considerably, in contrast to the pathologic identity of the lesions of the endocrine organs. Cachexia was absent in all 4 patients, but all of them presented a dry squamous skin and loss of axillary and pubic hair. In only 1 was myxedema simulated by manifestations of thyroid insufficiency.

Acta Medica Scandinavica, Stockholm

124:315-416 (June 1) 1946

One of the Forms of Anemia Splenica and Function of Spleen. C. D. de Langen.—p. 315.
*Adenoma of Islets of Langerhans and Pregnancy. A. W. M. Pompen, C. A. L. Jansen and J. Dhont.—p. 334.
Nerve Excitability and Occurrence of Tetanic Symptoms During Pregnancy and Lactation. L. Kirstein and E. Kugelberg.—p. 348.
Giant Follicle Lymphadenopathy (Follicular Reticulosis—Brill-Symmer's Disease). F. Heintzelmann.—p. 359.
Basis of Renal Kinetic Theory: X. G. Ekehorn.—p. 379.
Case of Periarteritis Nodosa. A. Homb.—p. 404.

Adenoma of Islands of Langerhans and Pregnancy.—Pompen and his associates report the case of a 35 year old woman with hyperinsulinism caused by an adenoma of the islands of Langerhans. Repeated attacks of hypoglycemia with loss of consciousness accompanied by profuse perspiration and salivation occurred for the first time thirteen days after the delivery of her second child. Repeated determinations of the blood sugar showed low values varying between 0.50 and 0.60 per thousand. Minor complaints could be suppressed by administration of sugar. Half way through the third pregnancy definite improvement set in, and a constant intake of sugar to avoid symptoms was no longer necessary. Nine days after the delivery a severe attack of unconsciousness occurred lasting twelve hours. A tumor in the head of the pancreas of a diameter of 1.5 cm. and weighing 3 Gm. was removed surgically. Microscopic examination revealed an islet cell tumor. Sensitiveness to excess of insulin produced by the organism may be decreased during pregnancy. A glycotropic (anti-insulin) substance of the anterior pituitary gland may account for the peculiarity in the behavior of hyperinsulinism caused by the adenoma of the islands of Langerhans during pregnancy. The glycotropic factor may assure an uninterrupted supply of dextrose to the growing fetus.

V 132
1946

Book Notices

Annual Reprint of the Reports of the Council on Pharmacy and Chemistry of the American Medical Association for 1945, with the Comments that Have Appeared in The Journal. Cloth. Price, $1. Pp. 122. Chicago: American Medical Association, 1946.

This volume again points up the shift in emphasis of the Council's work: whereas formerly the Council was chiefly concerned in warning physicians against useless or dangerous preparations which they were being importuned to use, the Council's effort now is to offer instruction to physicians in the latest development in drug therapy and the status of the newer procedures and agents available for use. Not a single report on the unacceptability of a preparation appears in this volume if one excludes the general condemnation of cosmetics containing hormones contained in the report on that subject; however, this class of preparations is offered not so much to physicians as to the general public.

Two reports of meetings of the Council appear, one in October 1944 and the other in March 1945, the former being the regular meeting of the Council. These reports again emphasize the educational nature of the Council's work and bear witness to its leadership in the consideration of current therapeutic problems.

Wartime medical experience is the background of the report "Dermatophytosis: Treatment and Prophylaxis," which gives a concise estimate of progress in this field and sets up an admirable set of standards for the evaluation of fungicidal preparations. Of similar background is the report on "Dangers from the External Use of Sulfonamides," which conveys a warning against the over-the-counter sales. Another noteworthy report is that on the "Status of Poison Ivy Extracts," which emphasizes the fact that the value of available preparations is to be found in prevention rather than in treatment. The report on the Status of Acne Bacillus Vaccine points out that the character of this bacillus is that of a saprophyte and not a pathogen, and that preparations of it failed to arrest or control acne vulgaris in most cases.

The publication of the valuable report on pertussis vaccine prepared by Dr. Harriet Felton and sponsored by the Council prefaced the admission to New and Nonofficial Remedies of many preparations of this class.

The successive volumes of the Annual Reprint of Reports of the Council offer an extremely valuable source of reference material on the problems of drug therapy which have confronted the medical profession since the year 1905. The volume is available in medical libraries; the limited number of copies printed each year has perhaps regrettably prevented its wide distribution.

An Introduction to Biochemistry. By William Robert Fearon, M.A., Sc.D., M.B., Professor of Biochemistry, University of Dublin. Third edition. Fabrikoid. Price, 21s. Pp. 569, with illustrations. London: William Heinemann Medical Books, Ltd., 1946.

This book indeed lives up to its title as an introductory work in biochemistry and at the same time includes information that will appeal to the graduate as well as undergraduate student of the subject. The third edition establishes the book as a British textbook and student reference work of high standard. It is said to place more emphasis than did former editions on subjects of special interest in clinical medicine. While this phase of the subject receives some attention, it cannot be considered sufficient to meet more than barely minimum needs of medical students. Yet brevity has not entirely sacrificed a surprising degree of completeness in the enumeration of essentials.

The most striking feature of this publication is its brevity and clarity of style. Of philosophic interest are the quotations that introduce each chapter and appear occasionally in other parts of the text. The first four chapters, comprising part I, cover elements and inorganic compounds; the remaining twenty-two, part II, organic biochemistry. There are two appendixes at the end: one comprises tables of food composition and brief descriptions of the characteristics of the chief types; the other, a brief description of biochemical reagents and a table of abbreviations and equivalents. The first chapter of part II concerns the classification and characteristics of organic compounds. It can thus be seen that the author first introduces the student to principles of inorganic and then organic chemistry before presenting material peculiar to biochemistry. Along with the usual phases of the subject there is included a new final chapter on tissue chemistry that introduces the student to histochemistry in relation to physiology and microscopic anatomy, a phase that is receiving increased attention.

An average number of references are cited in the text and are listed alphabetically at the end of most chapters. Chapter 6, on the carbohydrates or glucides, is a notable exception. British preferences of spelling are followed throughout. The format is exceptionally clear and readable. The text is replete with structural chemical diagrams and formulas to illustrate the derivations of reactive changes of biochemical compounds. Numerous tables to summarize information further enhance its usefulness to the student. The text, footnotes and references are comparatively free of error. The subject index at the end lists a minimum of terms and gives preference for chemical substances rather than general topics. Though in keeping with the overall modest proportions of the book, this section could be expanded to make it more useful for reference.

Taken as a whole, this book is admirably suited to the needs of beginning students of biochemistry and to a lesser degree fulfils the minimum requirements of laboratory workers in allied sciences as a handy reference work.

A Clinical Atlas of Sternal Bone Marrow. By Carl Reich, A.B., M.D., F.A.C.P., Associate Clinical Professor of Medicine, New York Medical College, New York. Boards. Pp. 32, with 25 illustrations. North Chicago, Illinois: Abbott Laboratories, 1946.

This atlas was published as a service to the medical profession by Abbott Laboratories. There is a short introductory statement concerning the diagnostic importance of investigating the sternal bone marrow and the author's volumetric technic with detailed step by step illustration of the procedure. This is followed by a diagram of the cellular development in the normal marrow together with a description of the morphology of the individual cells. Next there are twenty-four colored plates of microscopic fields of characteristic pathologic marrow patterns with a key diagram of the field below to enable the reader to identify the cells. Under each plate is a terse summary of the essential features of the disease with its accompanying marrow pattern. The idea of an atlas of sternal marrow for the practitioner is an excellent one, but it is unfortunate that this publication was not more carefully edited before it went to press. In the first place the feasibility of aspirating 4 cc. of "bloody fluid" can be seriously questioned, as withdrawing such an amount results in admixture with peripheral blood and relatively diminishes the number of marrow cells. The use of a small mastoid mallet to penetrate the outer sternal plate complicates the procedure unnecessarily and certainly would increase the anxiety on the part of the subject. Finally, using oxalate as an anticoagulant is not in keeping with obtaining the best morphologic detail of the cells aspirated, and the plates in the atlas are good testimony to this criticism. Few hematologists would condone this technic, since the morphologic detail is important in cell identification and the plates leave much to be desired. Very little nuclear detail is shown in the illustrations, and the cells have a "cooked" appearance. The plate on megaloblastic hyperplasia is particularly poor. There are also some important misleading illustrations that may result in misinformation. The plate on infectious mononucleosis shows the sternal marrow picture of atypical monocytoid lymphocytes, whereas the bone marrow in this disease is characterized by a myeloid hyperplasia and immaturity, and in spite of the large numbers of atypical lymphocytes in the peripheral blood the bone marrow is not involved in the disease. The error could result only from admixture with peripheral blood. This point is of some clinical importance, as sternal puncture is of diagnostic aid in differentiating benign (infectious mononucleosis) from malignant (leukemia) lymphocytosis. The plate on aplastic anemia may also be misleading. The author's plate shows three degenerated cells and a lymphocyte. Such a plate has no teaching value whatever. While the marrow may be almost completely acellular in some cases, others may show a cellular

or hypercellular marrow, and these are the ones with the good prognosis. Sternal marrow study reveals these facts and is of great aid to the physician in formulating his prognosis. The same is true for agranulocytosis, and this finding also was not indicated by the author. The author recognizes that hyperplasia of megakaryocytic, myeloid and erythroid elements occurs in polycythemia, but his plate on this disease is a poor illustration of that fact. The plates on acute leukemia lack sufficient nuclear detail to make them of great teaching value. Finally, it is unfortunate that such a great amount of time and money was spent without achieving the desired objective. The purpose and organization of the atlas are excellent, but photographic virtuosity is no substitute for scientifically accurate and faithful reproduction of morphologic detail in hematology. Colored photography in medical illustration loses its glamour to the scientist if important diagnostic detail is lost or if facts are obscured. This atlas poses the important question in medical illustration as to whether the camera with all its virtues does not have definite limitations in the faithful reproduction of cellular morphology in smears of the peripheral blood or bone marrow.

Acctanilid: A Critical Bibliographic Review. By Martin Gross, M.D., Research Assistant (Assistant Professor), Laboratory of Applied Physiology, Yale University, New Haven, Connecticut. With an introduction by Howard W. Haggard, M.D., Director, Laboratory of Applied Physiology, Yale University. Monographs of the Institute for the Study of Analgesic and Sedative Drugs, I. Cloth. Price, $3. Pp. 155, with 8 illustrations. New Haven, Connecticut: Hillhouse Press, 1946.

According to the author this monograph undertakes to review the voluminous literature on acetanilid in a critical fashion. The emphasis is placed on the reported toxicity of acetanilid, and the conclusion which appears to be reached is that this drug is much maligned. One might be willing to accept this conclusion at its face value if it weren't for two factors. The author appears to be extremely critical of all experimental and clinical work tending to show potential dangers from acetanilid, whereas he finds little fault with work tending to show the opposite. Secondly, the book was made possible by a grant from the Institute for the Study of Analgesic and Sedative Drugs, an institute founded and operated by members of the industry which promote acetanilid, aspirin, bromides and other sedatives and analgesics to the public. Nevertheless the book is valuable as a compilation of the literature on this drug, and the cross references at the end of each chapter are exceedingly well done.

La acción diabetógena de la hipófisis. Por Alberto B. Houssay. Tesis para optar al título de doctor en medicina. Universidad nacional de Buenos Aires, Facultad de ciencias médicas, Escuela de medicina. Paper. Pp. 144, with 11 illustrations. Buenos Aires: Sebastián de Amorrortu e Hijos, 1945.

This thesis by the son of the renowned Argentinean physiologist is a comprehensive review of our knowledge concerning the diabetogenic action of the anterior pituitary lobe. The book is divided into three sections. The first deals with the history of our concepts of the role of the hypophysis in carbohydrate metabolism. The second is a detailed analysis of the metabolic actions of the anterior pituitary of the toad. This animal has been used extensively by the Houssay school for endocrine investigations. The last section deals with mammalian pituitary physiology in its metabolic aspects. The bibliography is excellent and well arranged. The index is poor. In view of the unsettled conditions in Argentina in the past several years, it is interesting to note that the author remarks in his preface that 'the development of science is defective or impossible without liberty, and culture rapidly decays when liberty is restricted.'

Die spezielle Pathologie und die verletzungen der Mundgebilde für Ärzte, Zahnärzte und Studierende der Medizin und der Zahnheilkunde. Von Prof. Dr. Med. A. Fonio, Professor für Chirurgie an der Universität Bern. Bern. Cloth. Price, 12.80 Swiss francs. Pp. 200, with illustrations. Berne: Hans Huber, 1945.

The author attempts to cover special pathology of the oral cavity and related structures in a small volume. There is a severe lack of illustrations. The references are too few, with none to American literature. This book amounts to little more than a catalogue of conditions occurring in the oral cavity without further contributions.

The Health of the School Child. By Gertrude E. Cromwell, R.N., M.S., Supervisor Bureau of Health Education and School Nursing, Des Moines Public Schools, Des Moines, Iowa. Cloth. Price, $2.50. Pp. 256, with 46 illustrations. Philadelphia & London: W. B. Saunders Company, 1946.

Written primarily as a guide for the school nurse, this volume will be of equal interest and assistance to administrators, teachers and physicians because it presents the overall problems so completely and accurately and at the same time offers sound recommendations for action. It corrects effectively the misconception that so often arises that the school nurse operates exclusively in her little sphere and has no concern with other parts of the school system. The author emphasizes repeatedly the various ways in which child health work can be made a living, progressive program and not simply a "quick once over" at stated intervals, data from which are consigned to oblivion. This is especially well demonstrated in the chapter on use of the findings of the school medical appraisal, which deals extensively with acceptable printed forms. Handling of the communicable disease problem, another subject which is not well understood by many with school contacts, is outlined in another chapter. A unique approach is found in the chapter on teaching the child to care for himself, which the author introduces as "a theory of health education." That this should be the ultimate aim of health education is obvious but all too often forgotten. Helpful tabulations of information for children, the outcome of the teaching, and suggested activities and sources of information add to the value of the chapter. It is appropriate that one of the longest chapters of the volume is devoted to detailed discussion of the nursing program, with outlines of general duties, keeping of health records, nurse-teacher and nurse-parent contacts and the like. Also discussed are the specialized, generalized and rural school nursing services. The final chapter presents important details by which results of school health supervision may be evaluated. This book is a valuable contribution especially at this time, when health education is assuming much more significance.

V 132
1946

Occupational Therapy for the Limbless. By Phyllis Lyttleton, C.S.P., M.A.O.T. Paper. Price, 3s. Pp. 40, with drawings by Joan Harry. London: H. K. Lewis & Co. Ltd., 1946.

In the rehabilitation program of the injured members of the armed forces a great amount of attention has been devoted to occupational therapy. Furthermore, there has been an introduction of new ideas into the selection of the crafts which are laid out for the injured person to do as an exercise. For example, the modern occupational therapy technician does not expect the patient to weave baskets, make rugs and do light woodwork exclusively; he may enter into assembling electrical equipment such as radios and amplifiers or may work in the machine shops or on engines and motors, doing things which may be of interest. This booklet offers an additional selection of crafts for a patient who is more interested in the finer arts. The booklet, of course, is especially designed for assisting occupational therapy technicians who are treating the limbless. Therefore, various arts and crafts are proposed which are intended to give the right kind of exercise and to help train the handicapped persons to use their prosthesis. The booklet also deals with the psychologic as well as the physical approach.

Lippincott's Quick Reference Book for Medicine and Surgery: A Clinical Diagnostic and Therapeutic Digest of General Medicine, Surgery, and the Specialties, Compiled Systematically from Modern Literature. By George E. Rehberger, A.B., M.D. Thirteenth edition. Fabrikoid. Price, $15. Pp. 1,461, with 464 illustrations. Philadelphia, London & Montreal: J. B. Lippincott Company, 1946.

This compendium has been appearing in new editions at frequent intervals since 1920. It is in essence a short encyclopedia of medicine. Because of the necessity of condensation and the rapid advances in medicine, the book is not completely satisfactory in all respects. Under the heading endocarditis, for example, four types are considered together: rheumatic, syphilitic, bacterial and "indeterminate." Under treatment of "endocardtis" mercurochrome is mentioned as having value, but there is no mention of penicillin. A brief discussion of penicillin, however, is contained in the alphabetical list of drugs which forms part II of the book. As a source for quick though superficial reference this volume continues to have merit.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

ADMINISTRATION OF TETANUS ANTITOXIN

***To the Editor:*—Is the administration of prophylactic antitetanic serum as effective if given the day following an injury as at the time of the initial wound?**

M.D., Illinois

ANSWER.—To prevent tetanus it is desirable to inject an adequate dose of antitetanic serum as early as possible after the injury. The success or failure of seroprophylaxis depends on the amount of tetanus toxin which becomes irreversibly fixed to the tissues of the central nervous system before the injection of antitetanic serum. Obviously, if the injury is one likely to be associated with a short period of incubation, a delay of one or more days would reduce the efficiency of the serum. On the other hand, the injection of antitetanic serum in circumstances in which the incubation period might be long would probably be completely effective despite a delay of one or more days. Clinically, however, it is impossible to predict the length of the incubation period. Among a group of 223 patients with known sites of infection admitted to the Cook County Hospital, Chicago (Spaeth, Ralph: Therapy of Tetanus, *Arch. Int. Med.* **68:**1133 [Dec.] 1941), the percentage distribution in respect to incubation periods was as follows:

Incubation period in days:

	2 to 5	6 to 10	11 to 15	16 to 20	21 to 30	34 to 85
Percentage:	20.7	43	21.5	5.8	7.2	1.8

Hence it is evident that under average circumstances the incubation period will be over five days in 80 per cent of the cases. The site of infection is not related to either the incubation period or the mortality rate.

In actual practice the dose of antitoxin for prophylactic purposes has ranged from 1,500 to 20,000 units. In order to avoid confusion and to cover most exigencies, a routine dose of 10,000 American units is indicated as a substitute for the 1,500 units commonly employed. Doses of 20,000 units are justified in the presence of either severe injuries or significant delay in seroprophylaxis. When doses of 20,000 units or more are employed, it is not necessary to make additional injections for any given injury.

Passive immunity, induced by the antitetanic serum, should be supplemented by active immunity through the use of tetanus toxoid. This end may be achieved by the properly timed inoculation of tetanus toxoid. The tetanus toxoid should be administered at a time when the passive immunity conferred by antitetanic serum has reached a minimal level. Such a procedure is dictated in terms of the basic principle that passive immunity quantitatively interferes with the development of active immunity (Cooke, J. V., and Jones, F. G.: The Duration of Passive Tetanus Immunity, THE JOURNAL, April 10, 1943, p. 1201). Since 10,000 units confers a passive immunity for six to ten weeks, the injection of tetanus toxoid is best deferred for this length of time. The dosage schedule of tetanus toxoid is that ordinarily recommended. Tetanus antitoxin does not confer persistent immunity, and the patient should be advised accordingly.

SIMPLE TEST FOR OCULAR DOMINANCE

***To the Editor:*—Please describe the simplest test for ocular dominance.**

M.D., Ohio.

ANSWER.—No simple test of ocular dominance is known which is consistently dependable. Too much dependence should not be placed on any one test. A battery of simple tests seems advisable, especially in cases of variable dominance or amphiocularity. One of the simplest tests is the hole-in-card test. A hole about the size of a dime is cut in the center of a piece of cardboard measuring about 5 by 8 inches. This is held first by the examiner in front of the patient's face with the hole so placed that the patient must move the head to one side or the other to see through it. Then the card is given to the patient to be held first in his lap and then raised to sight in position, first held in one hand, then in the other, and finally by both. The result of these four observations will generally give a fair estimate of the patient's ocular dominance.

POLLEN CONTENT IN SOUTHEASTERN DAKOTA

***To the Editor:*—What is the pollen content of the air at different seasons at Yankton, S. D.?**

B. A. Black, M.D., Grove City, Pa.

ANSWER.—Tree pollens appear in the air in limited quantities in southeastern South Dakota in March, April and May. The principal sources of tree pollens at Yankton are, in the order of their seasonal blossoming, elm, cottonwood, box elder, ash and willow. Grasses begin to shed pollen in moderate quantities from about the first of June until the middle of July. The principal sources of grass pollen are bluegrass and timothy. Brome grass (Bromus inermis) is a common cultivated grass in fields and on roadsides. Among the wild grasses the most abundant producer is western wheat grass (Agropyron smithii). Farmers may be exposed to the pollen of rye in June and of corn and Sudan grass in July and August.

The weed pollen season begins in early July and lasts until the end of September. Two distinct types of weeds are involved—Russian thistle and related genera and species and the ragweeds. Russian thistle, Mexican firebush (Kochia scoparia) and western water hemp (Acnida tamariscina) begin shedding pollen in early July, approximately a month ahead of the ragweeds, and continue into early September. Mexican firebush is very abundant and produces a large amount of pollen. Western water hemp is abundant only in moist river bottom land. Russian thistle is a weed of the dry uplands. The most conspicuous ragweeds in low ground are burweed marsh elder (Iva xanthifolia) and giant ragweed. Elsewhere short ragweed is dominant. Small amounts of hemp (Cannabis sativa) are found along the Missouri River but are probably not abundant enough to be regarded as an active factor. The ragweeds begin to shed appreciable amounts of pollen about August 10. Maximum atmospheric concentration is likely to occur during the last week of August or the first two days of September. No appreciable amount of pollen of any kind will be found in the air after the first of October. Among farmers there is some possibility of specific sensitization to sunflowers, as they are very abundant in fields in this area. Their season is August and September.

ADRENAL CORTEX EXTRACT FOR SECONDARY POLYCYTHEMIA

***To the Editor:*—What is the physiologic explanation of the symptomatic relief by adrenal cortical hormone in a patient with secondary polycythemia (chronic pulmonary disease or congenital heart disease)?**

M.D., New York.

ANSWER.—Secondary polycythemia usually results from chronic pulmonary disease in which there is interference of gaseous exchange in the lungs or from congenital heart disease in which venous blood from the right side of the heart is shunted into the arterial blood from the left side of the heart. In either case the arterial blood which reaches the bone marrow is incompletely oxygenated. The hemopoietic tissues respond to deprivation of oxygen by increasing the rate of formation of erythrocytes. This action leads in turn to an increased concentration of hemoglobin and erythrocytes in the peripheral blood. The phenomenon of increased hemopoiesis as a response to hypoxemia may be regarded as a desirable compensatory mechanism, and it is questionable whether an attempt should be made to relieve this sort of polycythemia unless the blood volume and blood viscosity have increased to the point of causing cardiac failure.

Subjective improvement of the patient should be questioned in the absence of careful hematologic studies as evidence that the secondary polycythemia was influenced by the administration of adrenal cortex extract. There is little likelihood that ordinary doses of adrenal cortex extract would produce any measurable effect in the human being with intact adrenal glands.

Large doses of adrenal cortex extract might possibly make the polycythemia more severe. Cushing's disease, now considered to be the result of an increased function of the adrenal cortex, is characterized by polycythemia. Administration of adrenal cortex extract then might be presumed to cause polycythemia or make existing polycythemia more severe. This phenomenon has not been observed. If adrenal cortex extract should prove to have the property of producing polycythemia, it might be effective in relieving the symptoms of the primary disease by increasing the oxygen carrying capacity of the blood.

Adrenal cortex extract has the property of increasing the plasma volume. Dilution then would cause a lowered concentration of erythrocytes, but the increased volume of plasma might make pulmonary congestion more severe.

Epinephrine, amphetamine sulfate and posterior pituitary injection have each produced polycythemia in animals, presum-

132
946

ably by constriction of the nutrient arterioles supplying the bone marrow. Adrenal cortex extract has not been shown to have such an action.

Therefore adrenal cortex extract would have little value in the treatment of secondary polycythemia.

TOXICITY OF RAW EGGS IN ULCER DIETS

To the Editor:—**In the therapy for duodenal ulcer are raw eggs, particularly the albumin, toxic? Are eggnogs containing raw eggs contraindicated in diets for patients with ulcer or with heart disease?**

George K. Herzog, M.D., San Francisco.

ANSWER.—Raw eggs consumed in any form are not considered toxic to patients with duodenal ulcer or ulcers elsewhere in the gastrointestinal tract. Certainly many such patients have eaten raw eggs generously without any known ill effect resulting.

Some persons, particularly children, are sensitive to egg albumin and manifest various allergic reactions following its ingestion. Similar allergic phenomena may occur in some persons following the ingestion of strawberries, shrimp or other foods. It is also known that undigested egg albumin as well as other undigested proteins may be absorbed from a presumably intact gastrointestinal tract and that this may occur more readily when there is a defect, such as a peptic ulcer, in the mucosa of the gastrointestinal tract (Marks, M. B.: *Am. J. Digest. Dis. & Nutrition* **3**:41 [March] 1936). When such absorption does occur, egg albumin which has a small molecule (molecular weight 35,000) compared to most other proteins, passes through the glomerular membrane without difficulty and is excreted in the urine, where it can be readily detected by the specific precipitin test.

The absorption and excretion of unaltered egg albumin is apparently not uncommon, and harmful effects do not result except when the egg albumin acts as an antigen. In the latter event one may manifest various allergic reactions after a subsequent ingestion of raw egg. Theoretically this might be expected to occur more frequently in patients with ulceration of the upper gastrointestinal mucosa. Actually this has not been reported to occur.

It may therefore be concluded that, in the absence of an allergic response, raw egg has no deleterious effect on patients with duodenal ulcer and that it need not be eliminated from their diet. The same statement also applies to the diet of cardiac patients.

RATIONALE OF THERAPY OF MEGACOLON

To the Editor:—**The answer on the treatment of Hirschsprung's disease in Queries and Minor Notes in The Journal, March 23, 1946, page 825, is puzzling. Neostigmine, like physostigmine, is a parasympathetic stimulant, and syntropan, like atropine, is a parasympathetic paralyzant, so that theoretically they oppose each other. Neostigmine is used to contract the intestine (as for postoperative gas pains) and syntropan to relieve spasm of the intestine or other smooth muscle. Furthermore, the use of spinal anesthesia (or sympathectomy) would indicate that a sympathetic paralyzant should be used rather than a stimulant. Neostigmine, as a parasympathetic stimulant to contract the intestine, should be indicated in megacolon. Since "parasympathetic paralyzants and sympathetic stimulants" are mentioned, neostigmine would not be included. It is assumed that spinal anesthesia is meant to inhibit only the craniosacral sympathetic nerves, without including the thoracolumbar sympathetic nerves, so that parasympathetic paralysis ensues (the craniosacral sympathetics being the parasympathetics). Perhaps the author meant to imply that any upset of the sympathetic balance would be of benefit in megacolon, so that, if neostigmine is not effective, syntropan or any other drug affecting any part of the sympathetic system should be used. Please clarify the rationale of treatment for megacolon.**

R. Mueller, M.D., Los Angeles.

ANSWER.—The nonsurgical treatment of megacolon is not on an entirely rational basis, probably because the pathologic characteristics of megacolon are not thoroughly understood. In advanced cases of megacolon there is a disturbance in the nerve plexuses the degree of which varies within wide limits. The action of the nerves supplying the large intestine is not constant. For this reason, in milder cases of megacolon treatment is designed to upset the sympathetic-parasympathetic balance in the hope that some benefit will accrue. A trial and error method is used; if a drug with one action does not give the desired effect, a drug with another action may give it. The proper treatment and the one which gives the best results in severe megacolon probably is partial resection of the colon. Reference is made to the article by Penick in THE JOURNAL, June 9, 1945, page 423, which states, in part, "The fact that both of these compounds [mecholyl bromide and syntropan], which have opposite effects, have given good results supports the often expressed contention that a perversion of the autonomic system is the fundamental fault." This may help to explain the apparent irrationality of the treatment.

NATURAL IMMUNITY TO TETANUS

To the Editor:—**How would you determine whether a person was refractory to tetanus?**

M.D., New York.

ANSWER.—Refractoriness or natural immunity to tetanus presupposes the presence of antitoxins in the tissues or the ability to elaborate antitoxin promptly and adequately in response to introduction of Clostridium tetani. However, Ramon states that man is incapable of acquiring a natural immunity against tetanus. Bergey, Brown and Etris were not able to find traces of antitoxin in the serums of 30 persons between 18 and 20 years of age or in the serums of 44 persons within 30 to 50 years of age. Furthermore, they point out that tetanus antitoxin is produced slowly in response to the first injection. A more striking demonstration of the absence of natural immunity is offered by Lahiri, who was not able to find even the slightest traces of tetanus antitoxin in the serums of 25 persons who were highly exposed to the risk of infection with Cl. tetani. The state of immunity to tetanus infection in a person who has been vaccinated against the disease can be evaluated by the determination of the antitoxin titer of his serum.

References:

Ramon, G.: L'anatoxine tétanique et la vaccination contre le tétanos, *Ann. de méd.* **42**: 358 (Oct.) 1937.

Bergey, D. H.; Brown, C. P., and Etris, S.: Immunization Against Tetanus with Alum Precipitated Tetanus Toxoid, *Am. J. Pub. Health.* **29**: 334 (April) 1939.

Lahiri, D. C.: Absence of Specific Antitoxin in Persons Exposed to Risk of Tetanus Infection, *Indian J. M. Research* **27**: 581 (Oct.) 1939.

BLOOD PRESSURE DURING NITROUS OXIDE ANESTHESIA

To the Editor:—**What effect does nitrous oxide anesthesia have on blood pressure during the period of its administration?**

A. M. Price, M.D., Charleston, W. Va.

ANSWER.—Controversy has arisen through failure to separate the effects of nitrous oxide from the effects caused by (1) inadequate dilution of nitrous oxide with oxygen, (2) obstructed respiration and (3) contraction of skeletal muscles. Nitrous oxide administered as an anesthetic agent through unobstructed air passages and with a minimum of 20 per cent oxygen has no effect on the blood pressure. Variations of blood pressure are noted during struggling in the second stage of anesthesia. With mild degrees of either hypoxia or accumulation of carbon dioxide there may be a rise of blood pressure as well as of the pulse and the respiratory rate. Severe degrees of hypoxia produce circulatory depression, characterized by a fall of blood pressure and a decrease of pulse rate with an end point of anoxia, cardiac arrest and, if not immediately corrected, death.

TOXIC EFFECTS OF CHLORINE GAS ON CENTRAL NERVOUS SYSTEM

To the Editor:—**Please give references on the acute and remote effects of chlorine gas poisoning on the central nervous system and pathologic findings in the brain.**

H. A. Osserman, M.D., New York.

ANSWER.—References to nerve tissue damage from chlorine are few in number and meager in detail, possibly because these changes are believed not to be prominent or because their study in general has been neglected. The reports are of cerebral anemia, probably through anoxemia, and venous congestion, hemorrhage and degenerate change. References include:

Chlorine: Occupation and Health, International Labour Office, Geneva, 1930, p. 432.

Klotz, O.: Acute Death from Chlorine Poisoning, *J. Lab & Clin. Med.* **2**: 889 (Sept.) 1917.

Hill, Leonard: Gas Poisoning, *Brit. Med. J.* **2**: 801 (Dec. 4) 1915.

Mott, F. M.: Punctiform Hemorrhages in the Brain in Gas Poisoning, *Proc. Roy. Soc. Med. London Path.*, 1917, p. 73 (2 cases described, type gas shell not told, evidently a pulmonary irritant).

CLIMATE FOR SINUSITIS

To the Editor:—**What is the best climate for a case of chronic frontal sinusitis?**

Carl O. Keck, M.D., Bethlehem, Pa.

ANSWER.—No one climate can be suitable for all persons suffering with varying grades of sinusitis. Hence it is necessary to test which location is favorable or unfavorable for any given patient.

If this patient is free of allergy, it might be well to consider Florida, southern California or Arizona. A vacation in one of these areas will permit the patient sufficient time to sample his new atmospheric environment before definite conclusions are drawn. He will probably find one of these areas beneficial.

V 132
1946